UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE: WELDING FUME PRODUCTS LIABILITY LITIGATION	:	**Case No. 1:03-CV-17000**
	:	**(MDL Docket No. 1535)**
	:	**JUDGE O'MALLEY**
	:	**ORDER**

With this Order, the Court rules on various pending *Daubert* motions. Although the Court's precise rulings as to each expert and each area of inquiry come with important explanations and caveats, the chart shown below presents a highly simplified summary of the Court's rulings. The Court's full discussion explains that, although most of the parties' *Daubert* motions are denied, the Court intends to restrict the scope of testimony of nearly all of the parties' experts.

Further, although the Court denies defendants' motion to exclude all testimony that welding fume exposure causes Parkinson's Disease, the Court may still grant a defense motion for judgment as a matter of law in a particular case if the Court is convinced that, given the precise constellation of symptoms and test results presented by an individual plaintiff, there is no reliable medical or scientific evidence upon which to base a conclusion that the plaintiff's actual condition was, more probably than not, caused by exposure to manganese in welding fumes.

Motion	Ruling
By Defendants To Exclude All Testimony That Exposure To Welding Fumes Causes Parkinson's Disease (docket no. 255)	**DENIED**
By Defendants To Exclude Testimony by Mr. Ewing and Dr. Zimmerman Relating to Issues of Medical Causation or Toxicology (docket no. 972.3)	**DENIED**
By Defendants To Exclude Testimony of Dr. Cunitz Regarding the Adequacy of Defendants' Product Warnings (docket no. 972.4)	**GRANTED IN PART AND DENIED IN PART**
By Defendants To Exclude Testimony of Dr. Roth and Dr. Parent Regarding the Absorption, Distribution and Fate of Manganese from Welding Fume Particles in the Human Body, or That Chronic Exposure to Welding Fume Causes Injury to the Central Nervous System (docket no. 972.5)	**DENIED**
By Defendants To Exclude Testimony of Dr. Wells Regarding the Methodology and Reliability of Epidemiology Studies of the Effects of Manganese Exposure in Humans (docket no. 972.6)	**DENIED**
By Defendants To Exclude Testimony of Dr. Levy Regarding: (a) What Defendants Knew or Should Have Known about the Neurological Effects of Manganese in Welding Fume; and (b) That Defendants Did Not Meet 'His Standard' of Occupational Health Practice (docket no. 972.7)	**DENIED**
By Defendants To Exclude Testimony of Dr. Hoffman, Dr. Levy and Dr. Zimmerman That Defendants Acted in an Unethical Manner (docket nos. 972.8 & 1012)	**GRANTED**
By Plaintiffs To Exclude the Testimony of Dr. Lees-Haley (docket no. 968)	**DENIED as moot, without prejudice**

CONTENTS OF THIS OPINION

I. Background.

Beginning in late 2004, the parties in this Multi-District Litigation ("MDL") provided each other with designations of their "core experts" – that is, experts who will offer "generally applicable" testimony in more than one of the MDL constituent cases.[1] Plaintiffs designated 17 core experts, and defendants designated 30 core experts; the areas of expertise include neurology, neuro-pathology, neuro-psychology, neuro-radiology, epidemiology, bio-statistics, industrial hygiene, industrial engineering, chemistry, materials science, warnings, corporate ethics, military specification and procurement procedures, economics, government lobbying, and ancient corporate documents.

Following deposition of these experts, the parties filed numerous motions invoking *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), arguing that some or all of the proposed testimony of some of these experts should be excluded. In addition to reviewing these briefs and the many attached exhibits,[2] the Court held a *Daubert* hearing over a period of several days. At this hearing, the parties presented argument and expert testimony, and questions were put to both the attorneys and the experts by the undersigned, by the MDL Special Master (David R. Cohen), and by the Special Master appointed to oversee the related state court litigation known as California Judicial Council Coordination

[1] *See* docket nos. 419 & 741 (plaintiffs' core expert designations), 622 (defendant Caterpillar's core expert designations), 623 (defendant GE's core expert designations), 628 (defendant Select Arc's core expert designations), 633, 1236 (defendant Lincoln Electric's core expert designations), 800 (defendant Metropolitan Life Insurance Company's core expert designations); *see also* docket nos. 624, 625, 626, 627, 629, 630, 631, 632 (cross-designation of core experts by various co-defendants). A list of all of the parties' designated core experts, showing whether each expert was challenged in a *Daubert* motion, is attached as Exhibit A.

[2] The parties and their affiants have cited to literally hundreds of medical and scientific articles and treatises, all of which have been provided to the Court on CD-Rom.

Proceeding No. 4368 (Honorable Owen Lee Kwong).[3]

Despite the extensive nature of this hearing, the parties agreed they would not address *all* issues relating to the admissibility of expert testimony that may arise in these MDL cases. There are additional proceedings relating to both other core experts and also case-specific experts which have yet to occur.[4] Thus, the Court issues this Order with the understanding that, while broad, it is not comprehensive.

II. The *Daubert* Standard.

For over 70 years, the "dominant standard for determining the admissibility of novel scientific evidence at trial" was known as the *Frye* test. *Daubert*, 509 U.S. at 585 (*citing Frye v. United States*, 293 F. 1013, 1014 (1923)). The *Frye* test held that "scientific evidence was admissible only if based on principles generally accepted as valid by the scientific community." Charles Wright & Victor Gold, 29 *Fed. Prac. & Proc. Evid.* §6266 at 265 (1997) ("Wright & Gold"). A problem with the *Frye* test, however, was that it "excluded cutting-edge scientific evidence that might be [1] both relevant and reliable under traditional legal standards but [2] was not yet widely accepted by scientists." *Id.* Thus, when Congress

[3] The Court invited state court judges who are presiding over related Welding Fume cases to attend the *Daubert* hearing, and two attended in person: Judge Kwong from California and Judge Ben Hardin from Angleton, Texas. Several other state court judges have accepted this Court's offer to receive digital videotapes and transcripts of the entire proceedings. Any judge who wishes to receive these videotapes/transcripts should contact this Court.

[4] Specifically, beginning on July 25, 2005, the Court will hear *Daubert*-related challenges in connection with the following pending motions, among others: (1) plaintiffs' motion to strike or limit testimony relating to PET scans (docket no. 964); (2) plaintiffs' motion to strike or limit the testimony of Laurence Fechter and Brian Buckley (docket no. 966); (3) plaintiffs' motion to strike or limit testimony regarding pathology (docket no. 971); (4) certain sub-parts of defendants' omnibus motion to exclude testimony and opinions of plaintiffs' core expert witnesses (docket no. 972); and (4) any motions directed at excluding testimony of experts specific to the first MDL trial (*Ruth v. A.O. Smith Corp.*, case no. 04-CV-18912).

enacted the Federal Rules of Evidence in 1975, it adopted a more liberal approach toward admitting scientific evidence. *See Daubert*, 509 U.S. at 588-89 (contrasting the "austere standard" of the *Frye* test to "the liberal thrust of the Federal Rules and their general approach of relaxing the traditional barriers to opinion testimony") (internal quotation marks omitted). In particular, Congress enacted Federal Rule of Evidence 702, which provides as follows:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

In *Daubert*, the Supreme Court made clear that Rule 702 replaced the *Frye* test, and further held that federal[5] district court judges are to serve a "gatekeeping role" – "the trial judge must ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable." *Daubert*, 509 U.S. at 589. Put differently, before admitting expert testimony, trial courts must assure that the three conditions set out in Rule 702 are met. The Supreme Court also suggested a non-exclusive list of factors for trial courts to consider when deciding whether proposed scientific[6] expert testimony is sufficiently "reliable," as required by the second and third conditions in Rule 702. The specific factors listed by the *Daubert* Court are: "(1) whether the expert's technique or theory can be or has been tested – that is, whether the expert's theory can be challenged in some objective sense, or whether it is instead simply a subjective,

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[5] While many states have also adopted the *Daubert* approach as the standard for admissibility of scientific evidence, several states have explicitly declined to adopt *Daubert* and instead continue to adhere the the *Frye* test, or to some other standard. *See* 29 Wright & Gold at §6266 nn.22-23 (citing cases).

[6] In *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 147 (1999), the Supreme Court added that the "basic gatekeeping obligation" discussed in *Daubert* applies not just to "scientific" testimony, but to "all expert testimony," including technical or other specialized expert testimony.

conclusory approach that cannot reasonably be assessed for reliability; (2) whether the technique or theory has been subject to peer review and publication; (3) the known or potential rate of error of the technique or theory when applied; (4) the existence and maintenance of standards and controls; and (5) whether the technique or theory has been generally accepted in the scientific community." Fed. R. Evid. 702 (advisory committee notes, 2000 amendments) ("*Advisory Committee Notes*"); *Daubert*, 509 U.S. at 593-594. Notably, *Daubert* itself "emphasized that the[se] factors were neither exclusive nor dispositive," and "other cases have recognized that not all of the specific *Daubert* factors can apply to every type of expert testimony." *Advisory Committee Notes*. The Court has "considerable leeway in deciding in a particular case how to go about determining whether particular expert testimony is reliable." *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999).[7]

In addition to the non-exhaustive list of factors identified explicitly in *Daubert*, other courts have recognized at least five other factors relevant to the determination of whether expert testimony is sufficiently reliable to be admitted into evidence. *See generally Advisory Committee Notes* (listing these five factors). One such factor is whether the field of expertise claimed by the expert, even if it is "generally accepted," is known generally to reach reliable results at all. *See Kumho Tire Co. v. Carmichael*, 526 U.S 137, 151 (1999) (*Daubert's* general acceptance factor does not "help show that an expert's testimony is reliable where the discipline itself lacks reliability, as for example, do theories grounded in any so-called generally accepted principles of astrology or necromancy"); *Moore v. Ashland*

[7] *See also Kumho*, 526 U.S. at 142 ("the law grants a district court the same broad latitude when it decides *how* to determine reliability as it enjoys in respect to its ultimate reliability determination") (emphasis in original); *Hollander v. Sandoz Pharmaceuticals Corp.*, 289 F.3d 1193, 1206 (10th Cir. 2002), *cert. denied*, 537 U.S. 1088 (2002) ("when coupled with th[e] deferential [abuse of discretion] standard of review, *Daubert's* effort to safeguard the reliability of science in the courtroom may produce a counter-intuitive effect: different courts relying on . . . essentially the same science may reach different results") (citing Federal Judicial Center, *Reference Manual on Scientific Evidence* at 27 (2nd ed. 2000)).

Chemical, Inc., 151 F.3d 269 (5th Cir. 1998) (en banc) (clinical doctor was properly precluded from testifying to the toxicological cause of the plaintiff's respiratory problem, where the opinion was not sufficiently grounded in scientific methodology); *Sterling v. Velsicol Chem. Corp.*, 855 F.2d 1188 (6th Cir. 1988) (rejecting testimony based on "clinical ecology" as unfounded and unreliable). Another critical factor is whether the expert has adequately accounted for obvious alternative explanations. *See Claar v. Burlington N.R.R.*, 29 F.3d 499 (9th Cir. 1994) (testimony excluded where the expert failed to consider other obvious causes for the plaintiff's condition); *cf. Ambrosini v. Labarraque*, 101 F.3d 129 (D.C. Cir. 1996) (the possibility of some uneliminated causes presents a question of weight, so long as the most obvious causes have been considered and reasonably ruled out by the expert).

Courts may consider also whether the expert proposes "to testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions expressly for purposes of testifying." *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995). Similarly, it is important to assess whether the expert "is being as careful as he would be in his regular professional work outside his paid litigation consulting." *Sheehan v. Daily Racing Form, Inc.*, 104 F.3d 940, 942 (7th Cir. 1997); *see Kumho Tire*, 526 U.S at 152 (*Daubert* requires the trial court to assure itself that the expert "employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field"). And the court must not admit expert testimony if the expert "has unjustifiably extrapolated from an accepted premise to an unfounded conclusion." *Advisory Committee Notes*; *see General Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) (noting that, in some cases, a trial court "may conclude that there is simply too great an analytical gap between the data and the opinion proffered").

The fifth factor identified by the Advisory Committee is that the trial court "must scrutinize not

only the principles and methods used by the expert, but also whether those principles and methods have been properly applied to the facts of the case." *Advisory Committee Notes*. As the court noted in *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717 (3rd Cir. 1994), "any step that renders the analysis unreliable . . . renders the expert's testimony inadmissible. This is true whether the step completely changes a reliable methodology or merely misapplies that methodology." *Id.* at 745. An expert may not begin with accepted principles only to reach his ultimate opinion through "conjecture, hypothesis, subjective belief, or unsupported speculation." *Wehling v. Sandoz Pharmaceuticals Corp.*, 162 F.3d 1158, 1998 WL 546097 at *5 (4th Cir. Aug. 20, 1998).

Critically, when the Court applies all of these factors in its role as gatekeeper, it "need not and should not determine the scientific validity of the conclusions offered by an expert witness. Rather, to decide admissibility the trial judge should only consider the soundness of the general scientific principles or reasoning on which the expert relies and the propriety of the methodology applying those principles to the specific facts of the case." 29 Wright & Gold §6266 at 271-72. Thus, if a court "rules that [a certain] expert's testimony is reliable, this does not necessarily mean that contradictory expert testimony is unreliable. [Rule 702] is broad enough to permit testimony that is the product of competing principles or methods in the same field of expertise." *Advisory Committee Notes*. *See Ruiz-Troche v. Pepsi Cola Bottling Co.*, 161 F.3d 77, 85 (1st Cir. 1998) ("*Daubert* neither requires nor empowers trial courts to determine which of several competing scientific theories has the best provenance. It demands only that the proponent of the evidence show that the expert's conclusion has been arrived at in a scientifically sound and methodologically reliable fashion."). The flexibility of the *Daubert* inquiry "gives the district court the discretion needed to ensure that the courtroom door remains closed to junk science, while admitting reliable expert testimony [– even competing expert testimony –] that will assist the trier of fact."

Amorgianos v. Nat'l R.R. Passenger Corp., 303 F.3d 256, 267 (2nd Cir. 2002).

Since the admissibility of expert testimony is an issue to be resolved by the trial judge under Fed. R. Evid. 104(a), the Court "need only find by a preponderance of the evidence that the expert's reasoning and methodology is scientifically valid." 29 Wright & Gold §6266 at 276 (citing *Bourjaily v. United States*, 483 U.S. 171, 175 (1987)). Rule 104(a) serves to underscore that "*Daubert* does *not* require that a party who proffers expert testimony carry the burden of proving to the judge that the expert's assessment of the situation is correct." *Ruiz*, 161 F.3d at 85 (emphasis added); *see Bonner v. ISP Technologies, Inc.*, 259 F.3d 924, 929 (8th Cir. 2001) ("it is the expert witnesses' methodology, rather than their conclusions, that is the primary concern of Rule 702"). Thus, under *Daubert*, "the rejection of expert testimony is the exception rather than the rule." *Advisory Committee Notes*. This is, in part, because the Supreme Court prefers that litigants rely upon "the capabilities of the jury and of the adversary system generally," rather than "wholesale exclusion" of fairly supported, relevant testimony by the Court. *Daubert*, 509 U.S. at 596. "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Id.* This principle remains true even in the most complicated cases: "As long as an expert's scientific testimony rests upon 'good grounds, based on what is known,' it should be tested by the adversary process – competing expert testimony and active cross-examination – rather than excluded from jurors' scrutiny for fear that they will not grasp its complexities or satisfactorily weigh its inadequacies." *Ruiz*, 161 F.3d at 85 (quoting *Daubert*, 509 U.S. at 590). The Court's role is "that of gatekeeper[, not] that of armed guard." *Id.* at 86.

A final point: in addition to examining an expert's methodology, the Court must examine an expert's qualifications. An expert may be highly qualified to respond to certain questions and to offer

certain opinions, but insufficiently qualified to respond to other, related questions, or to opine about other areas of knowledge. "When making a preliminary finding regarding an expert's qualifications under Fed. R. Evid. 104(a), the court is to examine 'not the qualifications of a witness in the abstract, but whether those qualifications provide a foundation for a witness to answer a specific question.'" *Smelser v. Norfolk Southern Ry. Co.*, 105 F.3d 299, 303 (6th Cir. 1997), *cert. denied*, 522 U.S. 817 (1997) (quoting *Berry v. City of Detroit*, 25 F.3d 1342, 1351 (6th Cir. 1994), *cert. denied*, 513 U.S. 1111 (1995)). "The trial court must determine whether the expert's training and qualifications relate to the [*specific*] subject matter of his proposed testimony." *Id.* Thus, for example, a witness qualified as an expert in cardiovascular pharmacology may be allowed to opine about how a drug affects the heart, but not on how obesity affects the heart. *In re Meridia Products Liab. Litig.*, 328 F.Supp.2d 791, 805 (N.D. Ohio 2004). A district court "must continue to perform its gatekeeping role by ensuring that the actual testimony does not exceed the scope of the expert's expertise, which if not done can render testimony unreliable under Rule 702." *Wheeling Pittsburgh Steel Corp. v. Beelman River Terminals, Inc.*, 254 F.3d 706, 715 (8th Cir. 2001).

Having set out the relevant standards for admissibility of expert testimony, the Court now turns to the arguments raised by the parties in this case.

III. Challenges To Specific Experts.

Before addressing each challenged expert individually, the Court makes this general observation. Both the plaintiffs' experts and the defendants' experts in this case are, to varying degrees, guilty of the same fault: they reach outside their area of expertise to opine about the ultimate issue of, for example, whether exposure to manganese in welding fumes can cause Parkinson's Disease or other neurological injury. As discussed in detail below, such an opinion is certainly within the area of expertise of some of

the parties' experts (e.g., neurologists), but clearly not within the area of expertise of other experts (e.g., chemists). Merely because a person is an expert and can assist the jury to understand discrete issues raised by the parties does not mean he must opine about *every* important issue in the case. On the other side of the coin, despite the parties' arguments otherwise, simply because a witness is not an expert about *everything* does not mean he is unqualified to offer expert opinion about *anything*.

Nearly all of the experts' reports reveal that they read many medical and epidemiological journal articles that studied and discussed the neurological effect of manganese. While this review may have been vital to those experts' understanding generally of the issues and background of this litigation, it does not make them experts on that particular subject. Still, a given expert's tendency to opine about areas outside of his particular expertise does not, by itself, disqualify him from testifying about his true, core area of expert knowledge. This litigation will be shorter and smoother if the parties tailor their presentations by ensuring each expert's opinion is so confined. The Court's discussion below should help make this distinction clear.

A. Dr. Cunitz.

Plaintiffs have designated Dr. Robert Cunitz to opine about the adequacy *vel non* of the manufacturers' warnings about the dangers of using welding rods. Dr. Cunitz received his doctorate degree in "Experimental and Human Factors Psychology." Dr. Cunitz explains that his training and background have given him expertise in "how human beings perceive and react to environmental stimuli. This specialized knowledge concerns human visual and auditory perception, comprehension of language and symbols, . . . human learning, attention and motivation, the elements necessary for visibility, and visual contrast and acuity." Declaration at ¶3. Among other positions, Dr. Cunitz has served as head of

the Human Factors Section in the Center for Consumer Product Technology of the National Bureau of Standards, and is a member of the American National Standards Institute ("ANSI"), Z535 Committee on Warning Signs and Colors. Dr. Cunitz asserts that his specialized background and knowledge allows him to "assess [1] the risks inherent in a product, [2] the need to warn against such risks and instruct in the use of the product, and [3] how to make warnings and instructions most effective to the intended users of such products." *Id.* The Court concludes, however, that Dr. Cunitz is qualified to opine in this case about only the last of these three matters.

In his report, Dr. Cunitz states he reviewed documents and opinions of *other* experts which reveal: (1) the causal connection between welding and neurological injury; (2) manufacturers' knowledge of the hazards of welding fumes; and (3) public perception of these hazards. This review allows him to "determin[e] (a) if warnings were necessary; (b) if warnings would be effective; (c) if there are risks of serious injury associated with a hazard; (d) the nature of the warnings necessary; (e) the appropriate manner in which to communicate the warnings and the conspicuity necessary so the warnings would be read; and (f) whether it is necessary to put permanent warnings on the product itself rather than only in material which accompanies the product." *Id.* at ¶10. But in the context of this case, determinations (a)-(d) above are not within Dr. Cunitz's own area of expertise. For example, the questions of whether certain "warnings were necessary," and how much "risk[] of serious injury [is] associated with a hazard," depend primarily on whether, or the degree to which, welding fumes cause neurological injury; at best, Dr. Cunitz can only rely on the opinions of other experts to answer this question. Dr. Cunitz is not, himself, qualified

to opine on whether welding fumes cause neurological injury.[8] The parties have many other experts who can and will opine on this issue. Similarly, Dr. Cunitz is not qualified, in this case, to opine about the degree of the manufacturers' knowledge of hazards associated with welding fumes, or about what plaintiffs would have done had they been given different warnings.[9]

Moreover, several (but not all) aspects of Dr. Cunitz's opinions either mis-state the applicable legal standards or invade the province of the jury. For example, Dr. Cunitz explains that "warnings are necessary" if, among other things, the manufacturer has a "reasonable suspicion of harm," meaning that "prudent inquiry" by the manufacturer would reveal "*a possibility* that danger may be present during the foreseeable use or misuse of [the] product." *Id.* at ¶25 (emphasis added). This is simply not the correct legal standard – knowledge of a mere "possibility of danger" does not necessarily translate to a legal

[8] While it us true that Federal Rule of Evidence 703 allows an expert to rely on hearsay, including the opinions of other experts, any such reliance does not enlarge the witness's fundamental area of expertise. Dr. Cunitz is not a neurotoxicologist, and he does not become qualified to offer neurotoxicological causation opinions merely because he read the declarations of other experts. *See Larson v. Kempker*, 405 F.3d 645 (8th Cir. 2005) ("an expert may extrapolate from data supplied by other experts . . . , but a person does not become an expert simply by reviewing any expert's reports or research")

[9] Defendants correctly point out that Dr. Cunitz is not qualified to opine about these particular issues because he supplies no methodology addressing the foundation for these opinions.

warning requirement, nor does it necessarily imply liability.[10]

Dr. Cunitz also proposes to offer "ultimate question" testimony that various warnings were ineffective and inadequate. It is true that, under Federal Rule of Evidence 704(a), an expert opinion is not objectionable merely because it "embraces an ultimate issue to be decided by the trier of fact." But Rule 704(a) "does not lower the bar so as to admit all opinions" – an evidentiary problem remains if "testimony containing a legal conclusion is allowed, as it may convey a witness's unexpressed, and perhaps erroneous, legal standards to the jury." *United States v. Smith*, 2003 WL 21675340 at *5 (6th Cir. July 15, 2003), *cert. denied*, 540 U.S. 976 (2003) (citing *Torres v. County of Oakland*, 758 F.2d 147, 150 (6th Cir. 1985)). "Moreover, testimony of an expert that constitutes mere personal belief as to the weight of the evidence invades the province of the jury." *Indiana Ins. Co. v. General Elec. Co.*, 326 F.Supp.2d 844, 847 (N.D. Ohio 2004) (citing *McGowan v. Cooper Indus., Inc.*, 863 F.2d 1266, 1273 (6th Cir.1987)). Because many aspects of Dr. Cunitz's opinions of warning adequacy are improperly premised upon, among other things: (1) an erroneous "possibility of danger" standard, and (2) his conclusion on the weight of the evidence regarding the neurological risks of inhaling welding fumes, they are inadmissible. *See Tyler By and Through Tyler v. Sterling Drug, Inc.*, 19 F.Supp.2d 1239, 1245 (N.D. Okla. 1998) (granting a motion to

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[10] *See, e.g.*, Ohio Rev. Code §2307.76(A)(1)(a) ("a product is defective due to inadequate warning or instruction if * * * the manufacturer *knew or, in the exercise of reasonable care, should have known* about a risk that is associated with the product," and failed to warn of that risk) (emphasis added); Miss. Code. §11-1-63(c)(i) ("In any action alleging that a product is defective because it failed to contain adequate warnings or instructions * * * , the manufacturer or seller shall not be liable if the claimant does not prove by the preponderance of the evidence that * * * *the manufacturer or seller knew or in light of reasonably available knowledge should have known* about the danger that caused the damage for which recovery is sought and that the ordinary user or consumer would not realize its dangerous condition") (emphasis added); *Caruolo v. John Crane, Inc.*, 226 F.3d 46, 51 (2nd Cir. 2000) ("Under New York law, a manufacturer has a duty to warn against latent dangers resulting from foreseeable uses of its product of which it *knew or should have known*") (emphasis added, internal quotation marks omitted). These "knew or should have known" standards are quite different from Dr. Cunitz's standard of "prudent inquiry would reveal a possibility of danger."

exclude Dr. Cunitz from offering similar opinions).

This is not to say, however, that all aspects of Dr. Cunitz's opinions fail to satisfy the dictates of Rule 704 and *Daubert*. For example, Dr. Cunitz opines that: (1) "many users did not see the packaging warnings because of their location on the package and because of the nature of * * * many workplace environments (tool or supply rooms where the rods were separated from the packaging before being handed out to welders);" and (2) an effective warning should have included certain words, symbols, and colors. Declaration at ¶30(d). These particular opinions are squarely within Dr. Cunitz's area of expertise (human factors psychology), and the Court's review of all the legal standards recited above mandates the conclusion that they are admissible under *Daubert*.

Ultimately, then the Court must **deny** defendants' motion to exclude *all* of Dr. Cunitz's expert opinions. On the other hand, as discussed above, certain of Dr. Cunitz's opinions are inadmissible, so the motion is also **granted in part**. It is difficult for the Court to provide in advance complete guidance to the parties as to "where the lines will be drawn" at trial. This is especially true because some of counsel's questions to Dr. Cunitz may be phrased in hypothetical form, some may refer to other testimony and evidence, and the Court will have to examine the overall methodological foundation for many of Dr. Cunitz's answers on a question-by-question basis. The parties will have to use the familiar trial technique of raising objections to particular questions.

As a general matter, the Court will circumscribe Dr. Cunitz's testimony to matters directly linked to human factors psychology. While Dr. Cunitz may rely on opinions of other experts regarding other issues in dispute (e.g., whether manganese in welding fumes causes neurological damage), or hypothetically assume certain facts, he may not opine about any issue not within his area of personal

expertise. As with every expert, he may not opine about every important issue in the case.[11]

Finally, the Court adds a word about the defendants' warnings expert, Dr. Richard Krenek. At the *Daubert* hearing, plaintiffs urged that any weaknesses in Dr. Cunitz's opinions were present, in at least equal degree, in Dr. Krenek's opinions. Plaintiffs stated they sought to "imply" that, if the Court limits Dr. Cunitz's testimony, it should similarly limit Dr. Krenek. As defendants noted in response, the reason that plaintiffs merely "implied" this position, rather than argued it outright, is that plaintiffs did not actually file a *Daubert* motion seeking to exclude any of Dr. Krenek's opinions. That plaintiffs did not file a *Daubert* motion regarding Dr. Krenek, however, does not, in practice, leave him without testimonial restriction.[12] All of the evidence rules still apply, and the Court will sustain any well-taken objection to questions soliciting Dr. Krenek's testimony on matters that are without foundation, premised upon the wrong legal standard, or outside his area of expertise. Defendants can expect that the scope of Dr. Krenek's and Dr. Cunitz's testimony will be equally restricted.

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[11] The Court examined all of the sub-parts of ¶30 of Dr. Cunitz's declaration, where he sets out his opinions, and attempted to identify which opinions would be admitted, and which would not. For the reasons stated above, the Court finds it cannot now rule categorically. As a general matter, however, and solely for the purpose of providing the parties with some soft guidelines, the Court is more likely to sustain an objection to the opinions expressed at ¶30(a, f, g, h, & i) than at ¶30(b, c, d & e).

[12] In fact, it is the Court's impression that many of the parties' "*Daubert* motions" are more in the nature of garden-variety motions in limine, seeking to ensure that experts will not be allowed to answer certain questions, whether because they are outside their expertise or otherwise. It is certainly appropriate for the parties to raise such evidentiary issues before trial. *See* 21 Charles Wright & Kenneth Graham, *Fed. Prac. & Proc. Evid.* §5037.1 at 95 (2005 Supp.) (noting that, among other benefits, motions in limine "le[a]d to better preparation of both court and counsel, [and] better evidentiary rulings at trial"). But it is fair to say that the issues raised in some of the parties' motions are not strictly *Daubert* arguments. *See, e.g., Diefenbach v. Sheridan Transp.*, 229 F.3d 27, 30 (1st Cir. 2000) (distinguishing between "an objection to the lack of proper qualifications to provide opinion testimony" and a challenge to "the 'scientific validity' underlying the testimony," and holding that the former is not a true *Daubert* challenge).

B. Dr. Zimmerman and Mr. Ewing.

Plaintiffs have designated as experts Dr. Neil Zimmerman and Mr. William Ewing, both of whom specialize in the field of Industrial Hygiene – that is, the identification, evaluation, and control of health risks in the workplace. Defendants have filed two separate motions arguing that Dr. Zimmerman and Mr. Ewing must be precluded from testifying about certain matters: one motion directed at excluding some of their opinions related to industrial hygiene (docket no. 972-1 at 66-87), and one motion seeking "an Order from the Court precluding Mr. Ewing and Dr. Zimmerman from testifying about medical causation and toxicology, which are beyond these witnesses' claimed area of expertise." Docket no. 972-3 at 1. The former motion is not yet ripe, and will be the subject of argument at the Court's July 2005 hearings.[13]

As to the latter motion, defendants note that neither Mr. Ewing nor Dr. Zimmerman are epidemiologists, toxicologists, or medical doctors. Defendants argue, accordingly, that these experts should not be permitted to offer the following opinions, because they are unqualified to do so:

1. "most welders, and safety and health professionals, do not recognize or appreciate the disabling and permanent injuries that can occur from inhaling welding fume and manganese," Ewing report at 7; *see also* Ewing depo. at 66 ("most welders do not know what manganese is or its health effects");

2. "the Occupational Safety and Health Administration's (OSHA's) [permissible exposure limit ("PEL")] for occupational exposure to manganese is not sufficiently protective of welder's health," Ewing depo. at 150; and

3. "based on the toxicology literature, the scientific literature, the case reports, * * * I believe firmly that manganese is a neurotoxin," Zimmerman depo. at 59, 66.

[13] The Court addresses in this section of the Order only Dr. Zimmerman's opinions regarding Industrial Hygiene, which is the subject of defendants' motion at docket no. 972-3. In section III.F of this opinion, below, the Court addresses Dr. Zimmerman's opinions regarding business ethics, which is the subject of defendants' motion at docket no. 972-8.

Motion at 3-4.[14]

The Court finds this motion is not well-taken. Neither Mr. Ewing nor Dr. Zimmerman come anywhere near making medical or diagnostic opinions that a particular welder suffered a particular injury from welding fume exposure. Nor do their opinions rely on toxicological or epidemiological expertise. Rather, the opinions listed above are entirely within their field of expertise – Industrial Hygiene – and the Court is satisfied that both men are qualified as experts in that particular field.

As an example, Mr. Ewing explains that his research into airborne hazards in the workplace, including welding fumes, began over 25 years ago, and he is a Fellow in the American Industrial Hygiene Association. Through his work, he gained a high degree of familiarity with how and why existing historical manganese exposure standards were determined, such as: (1) permissible exposure limits ("PELs") for manganese established by OSHA; (2) threshold limit values ("TLVs") for manganese established by the American Conference of Governmental Industrial Hygienists ("ACGIH"); and (3) recommended exposure limits ("RELs") established by the National Institute for Occupational Safety and Health ("NIOSH"). Mr. Ewing's work also required him to know that these governmental entities have identified manganese as a neurotoxin.[15] An expert industrial hygienist with Mr. Ewing's background is qualified to render the expert opinions identified above as objectionable by the defendants.

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[14] Although the Court denies the motion to exclude Dr. Zimmerman's testimony, it has some concern regarding the third numbered opinion set out above. It appears more appropriate for Dr. Zimmerman to opine that *the literature supports* the conclusion that manganese is a known neurotoxin; it does not appear that Dr. Zimmerman has sufficient medical or toxicological expertise to offer his personal belief that manganese is a neurotoxin.

[15] For example, the NIOSH Pocket Guide to Chemical Hazards specifically notes that symptoms of exposure to manganese include "Parkinson's; asthenia, insomnia, mental confusion; metal fume fever." One would expect an expert in Dr. Ewing's field to be familiar with this evidence. And, of course, defendants' own experts have also stated or written that manganese is a known neurotoxin.

It certainly remains true that the defendants may challenge Mr. Ewing's and Dr. Zimmerman's opinions through "[v]igorous cross-examination [and] presentation of contrary evidence." *Daubert*, 509 U.S. at 596, and may object to questions posed by plaintiffs' counsel, if appropriate. It is also true that Mr. Ewing and Dr. Zimmerman are not qualified to opine that manganese in welding fume causes Parkinson's Disease, and the Court would sustain an objection to a question asking them to so opine (as opposed to so assume). But Mr. Ewing and Dr. Zimmerman are qualified to give the opinions challenged in this motion by defendants, so the motion to exclude must be **denied**.

C. Drs. Roth and Parent.

Plaintiffs have designated as experts Dr. Jerome Roth, who is a toxicologist and biochemist, and Dr. Richard Parent, who is a toxicologist and chemist. With one motion, defendants challenge the qualifications of both doctors to render their opinions.

1. Dr. Roth.

Dr. Roth's declaration focuses on: (1) the mechanisms of human absorption of manganese particles found in welding fume, and (2) the subsequent distribution and effects of those particles in the human body. For example, Dr. Roth discusses in his report welding fume particle size, the solubility of these particles in the lung, the physiological mechanisms the human body uses to eliminate or absorb these particles, the amounts absorbed and eliminated, and the effect of these particles on the body and brain. Dr. Roth opines in particular detail regarding the physiological mechanisms that transport manganese

particles from the lungs to the brain.[16] Dr. Roth ends his declaration with the following ultimate opinion:

> [T]he net effect from chronic exposure to welding fumes is the increased deposition of manganese in the brain potentially causing a diffuse injury to the central nervous system, including the globus pallidus, substantia nigra, mid-brain, putamen, caudate, frontal cortex, pons and cerebellum.
>
> While some of the transport mechanisms discussed above are still being studied, there is no debate that manganese in welding fumes is bioavailable, does cross the blood-brain barrier and does cause neurologic injury.

Declaration at 7-8.

Defendants assert that Dr. Roth is not qualified to so opine, basing their argument on a litany of supposed deficiencies: (1) "he is not an expert in epidemiology, pulmonology, metallurgy, industrial hygiene, neurology, pathology, neuropsychiatry, movement disorders, or neuroimaging;" (2) he has "never conducted research involving living humans;" (3) he is "not a physician and does not see patients" and is "not qualified to diagnose" Parkinson's Disease; and so on. Motion at 2. Defendants also note particular weaknesses in his analysis, such as he: (1) "is not an expert on macrophages," (2) does not know the exact pH level inside the lysosome (where he asserts manganese particles are solubilized due to acidity), (3) is unaware of the exact physical structure or chemical makeup of manganese fume particles, and (4) does not know the proportion of manganese contained in the welding fume that finally enters the blood stream.

It is true that the gaps in an expert's base of knowledge, or in his analysis, can render his opinion

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[16] Dr. Roth describes two such lung-brain avenues. They are: *Avenue One* – (a) fume particles are moved from the lung, in mucus, to the digestive tract (through a process called the mucociliary escalator), then (b) absorbed through the intestine into the blood stream (by binding to a transport protein known as "divalent metal transporter 1," or "DMT1"), and (c) if not cleared from the body by the liver, move through an unknown mechanism to the endothelial cells lining the brain capillaries; and *Avenue Two* – (a) fume particles are surrounded in the lung by scavenger cells (pulmonary macrophages), then (b) dissolved inside lysosomes in those scavenger cells, (c) released into the lung fluid upon self-destruction of those cells, (d) transferred from the lung fluid to the blood stream by DMT1, and finally (e) transported across the blood brain barrier where deposition occurs. In other testimony, Dr. Roth has also described a third route: direct entry to the brain through the nasal cavity and olfactory system.

inadmissible. But the Court easily concludes that any lacunas identified by defendants in Dr. Roth's expert report are grist for cross-examination, not the basis for wholesale exclusion.[17] Dr. Roth's background in toxicology and biochemistry are impressive, including 30 years of laboratory research on neurotoxicity and neurochemistry, grants from the National Institutes of Health to study manganese biochemistry, and publication of nine articles in peer-reviewed scientific literature on manganese toxicity and transport. Using a grant from the Environmental Protection Agency ("EPA"), Dr. Roth spent four years studying specific mechanisms of manganese-induced neurotoxicity. That Dr. Roth is not *every* kind of expert and cannot opine about *every* aspect of the chemistry of manganese inside and outside the human body is probably not possible, and certainly not disqualifying. Further, the Court does not believe Dr. Roth has offered opinions outside his area of expertise. Importantly, for example, Dr. Roth stops short of opining that exposure from manganese in welding fumes causes Parkinson's Disease – he concludes only that exposure to welding fumes can lead to "increased deposition of manganese in the brain potentially causing a diffuse injury to the central nervous system." This opinion does not require expertise in epidemiology or neuropathology that Dr. Roth does not have.

With regard to Dr. Roth's concession that "some of the [manganese] transport mechanisms" he discusses are not fully understood, "[t]he fact that the mechanism remains unclear does not call the reliability of the opinion into question: 'Not knowing the mechanism whereby a particular agent causes a particular effect is not always fatal to a plaintiff's claim. Causation can be proved even when we don't

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[17] Defendants have moved separately for exclusion of certain of Dr. Roth's opinions as scientifically unreliable. *See* Omnibus Daubert Motion (docket no. 972) at 35 *et seq.* (arguing that there is no reliable scientific basis to support the opinion that certain physiological mechanisms, such as the olfactory transport system, allow manganese fume to reach the brain). The present motion, and this Order, are directed only at Dr. Roth's qualifications; defendants' other motions were not fully briefed in time for the Court's first *Daubert* hearing.

know precisely how the damage occurred, if there is sufficiently compelling proof that the agent must have caused the damage somehow.'" *In re: Phenylpropanolamine (PPA) Prods. Liab. Litig.*, 289 F.Supp.2d 1230, 1247 (W.D. Wash. 2003) (quoting *Daubert v. Merrell Dow Pharms., Inc.*, 43 F.3d 1311, 1314 (9th Cir. 1995) ("*Daubert II*")).[18] The Reference Manual on Scientific Evidence explains that toxicological evidence, among other things, "explains how a chemical causes a disease by describing metabolic, cellular, and other physiological effects of exposure." Federal Judicial Center, *Reference Manual on Scientific Evidence* at 403 (2nd ed. 2000). Dr. Roth's expert opinions are focused fairly narrowly on providing precisely that explanation. Further, he is qualified to provide those types of opinions, and his testimony is likely to aid the trier of fact. Thus, the Defendants' motion to disallow Dr. Roth as unqualified must be **denied**.

2. Dr. Parent.

Dr. Parent's report is much more wide-ranging than Dr. Roth's; while Dr. Roth focuses on physiological mechanisms involving the human body's uptake, processing, and transport of manganese in welding fumes, Dr. Parent's report is a broad overview of various types of research in manganese toxicity – mostly epidemiological research. Indeed, about half of Dr. Parent's 28-page report is devoted to an examination of the "Bradford Hill" criteria, which are "factors that guide epidemiologists" in making judgments about whether causation may be inferred from an association. *Reference Manual on Scientific Evidence* at 375 (citing A. Bradford Hill, *The Environment and Disease: Association or Causation?*, 58 Proc. Royal Soc'y Med. 295 (1965)).

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[18] *See also Daubert*, 509 U.S. at 590 ("Of course, it would be unreasonable to conclude that the subject of scientific testimony must be 'known' to a certainty; arguably, there are no certainties in science.").

In addition to epidemiology, Dr. Parent also provides an overview of research on, among other things: (1) government regulation of manganese exposure; (2) the content of welding fume generally, and manganese content in particular; (3) the levels of exposure to manganese experienced by welders; (4) the neurotoxicity of manganese found in welding fume; (5) symptoms of and differences between various neurological injuries (parkinsonisms); (6) the association between manganese exposure and these parkinsonisms, as revealed by epidemiology, neuropathology, and neuroimaging; and (7) the interplay of environment and genetics in causing parkinsonism. Dr. Parent's ultimate conclusion is that "inhalation exposure to manganese from welding fumes is causally related to the development of a continuum of neurological diseases referred to as parkinsonism or Parkinson's Disease." Report at 25.[19]

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[19] As explained below, the Court believes Dr. Parent tends to opine outside of his area of expertise when he offers opinions numbered 5, 6, and 7, above; the Court is more likely to sustain an objection at trial to questions seeking solicitation of such opinions.

Dr. Parent also offers the following 13 opinions (numbered by the Court) that lead up to his ultimate conclusion:

> [1] [E]xcessive inhalation exposure to manganese from inhalation of welding fumes can cause a parkinsonism that is similar, if not identical to, Parkinson's Disease (PD), but [2] presents at an early age as a result of environmental influence on a genetic template of mutations. It also should be clear from the citations presented above that [3] mild steel welding produces a working environment rich in manganese and [4] without protection a career welder would be exposed to high concentrations of manganese dust and fumes [5] in a particle size range that would result in particulate deposition in the deep lung. In addition, [6] other components of welding fumes would remain in the deep lung and [7] eventually dissolve and enter into general circulation in the blood stream either directly or via the lymphatic system and [8] eventually find their way to the brain via an active transport mechanism. [9] Once reaching the brain, manganese accumulates during continuing exposure and [10] causes injury to specific tissue in the basal ganglia region of the brain, the area known to be associated with regulation of movement and organization and expression of behavior sequences. [11] A sequella of symptoms closely resembling those of idiopathic PD follows. [12] Manganese compounds then clear the brain after exposure cases, but [13] the injury is progressive and irreversible even in the absence of manganese.

Report at 25. For the same reasons, the Court is more likely to sustain an objection to opinions numbered 1, 2, 11, 12, and 13 in this list.

The defendants complain that Dr. Parent "lacks the requisite knowledge, skill, experience, training, or education required under Rule 702" to render all of these opinions. Defendants note that, like Dr. Roth, Dr. Parent is not (and does not claim to be) "a medical doctor and is not an expert in epidemiology, pulmonology, metallurgy, industrial hygiene, neurology, neuropathology, neuropsychiatry, movement disorders, neuroimaging, or air modeling." Motion at 6. Defendants also note that Dr. Parent has not conducted any research in the field of Parkinson's Disease, nor published an article on the health effects of welding fumes. Ultimately, defendants assert that Dr. Parent is able to reach any conclusion at all only because he read hundreds of articles, and then adopted "bits and pieces" of them – "Dr. Parent's report essentially is a compilation of selected quotes from scientific literature." Motion at 8, 9. Defendants further assert that Dr. Parent often paraphrased inaccurately the "bits" that he adopted, and he simply and automatically rejected *other* "bits and pieces" from the same articles, if they did not support his predestined opinion.

It is true that a person does not become an expert in an area outside of his regular field merely by "reading up" for the specific purpose of testifying.[20] Indeed, Dr. Parent was disqualified for precisely this

[20] *See Wade-Greaux v. Whitehall Laboratories, Inc.*, 874 F.Supp. 1441, 1465, 1476 (D. V.I. 1994) (in assessing whether an expert witness who was a "pediatrician, pharmacologist and toxicologist" could testify, the Court stated: "Dr. Done's only knowledge or experience regarding the teratogenicity of sympathomimetics comes from his review, for purposes of testifying in litigation, of selected literature appearing in various publications and elsewhere. Accordingly, Dr. Done is not qualified to offer ultimate opinions as to the teratogenicity of sympathomimetics in humans.").

reason in another case.[21] But it is also true that a literature review is appropriate and helpful to a toxicologist. As the Federal Judicial Center explains:

> The basis of the toxicologist's expert opinion in a specific case is a thorough review of the research literature and treatises concerning effects of exposure to the chemical at issue. To arrive at an opinion, the expert assesses the strengths and weaknesses of the research studies. The expert also bases an opinion on fundamental concepts of toxicology relevant to understanding the actions of chemicals in biological systems.

Reference Manual on Scientific Evidence at 415. In other words, a literature review is fundamental to expression of expert toxicological opinion. Indeed, the foundation for an expert witness's opinion can be eroded by pointing out scientific literature with which he is *not* familiar. The question, then, is whether the expert's literature review is the *sole* basis for his opinion, or, instead, helps inform an opinion he reaches through his own experience, research, or tests in related arenas.

As defendants acknowledge, Dr. Parent is a Diplomate of the American Board of Toxicology,[22] a Fellow of the Academy of Toxicological Sciences, and a member of two European toxicology societies. He has made many dozens of presentations at national Toxicology meetings, including on the subject of "epidemiology for toxicologists;" has published extensively in peer-reviewed toxicology journals and

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[21] *See Poole v. Alfred J. Miller, General & Masonry Contracting Co.*, case no. 95-1260, slip op. at 2 (14th Jud. Dist. Ct. La. June 4, 1997) ("Dr. Parent admits his opinion regarding the toxicity of cement and cement dust is derived solely from the literature he researched for purposes of litigation. The propriety of allowing Dr. Parent to qualify as an expert simply to regurgitate the work of others is in itself questionable. * * * [Further, this] Court finds that the literature provided by Dr. Parent not only does not support his opinion, it refutes his opinion. Therefore, Dr. Parent is not even properly regurgitating the findings of others and stands alone in his opinion.").

[22] *See Reference Manual on Scientific Evidence* at 417 ("As of January 1999, 1,631 individuals from twenty-one countries had received board certification from the American Board of Toxicology, Inc. To sit for the examination, which has a pass rate of less than 75%, the candidate must be involved full-time in the practice of toxicology, including designing and managing toxicological experiments or interpreting results and translating them to identify and solve human and animal health problems. To become certified, the candidate must pass all three parts of the examination within two years.").

treatises; and acts as both editor and reviewer for several respected toxicology journals. There is little question that Dr. Parent is generally well-qualified as a toxicologist. As plaintiffs further note, from 1982-1986, Dr. Parent worked as a consultant for the American Welding Society (a now-dismissed defendant in this MDL), designing protocols for experiments examining the physiological effects of welding fumes. These experiments were primarily in the area of examining the toxicity of ozone gas given off during the welding process, but Dr. Parent explains that he "designed some studies that looked at not only the pulmonary toxicity of the fumes, but also, the mutagenicity and cytogenetics of welding fumes." Parent depo. at 44.[23] In 1985, Dr. Parent presented two papers at the Annual Meeting of the Society of Toxicology: "*In-vitro* Toxicity of Welding Fumes to Rat Alveolar Macrophages" and "Inhalation Toxicology of Welding Fumes." Curriculum Vitae at 8. This history shows that, unlike in the *Poole* case mentioned above at footnote 21, Dr. Parent has pursued his own research about the toxicity of the product in question, and did so outside of the context of his retention as an expert in the current litigation. Thus, there is a basis for plaintiffs' argument that Dr. Parent is qualified to speak specifically to the toxicology of welding fumes and to the strengths and weaknesses of studies done on that subject by others.

Defendants are correct that much of Dr. Parent's opinion is based on a review of the epidemiology literature, and not strictly the toxicology literature. The two fields, however, overlap:

> Clearly, both epidemiology and toxicology have much to offer in elucidating the causal relationship between chemical exposure and disease. *These sciences often go hand in hand in assessments of the risks of chemical exposure, without artificial distinctions being drawn between them.* However, although courts generally rule epidemiological expert opinion admissible, admissibility of toxicological expert opinion has been more controversial because of uncertainties regarding extrapolation from animal and in vitro data to humans. This particularly has been true in cases in which relevant epidemiological research data exist. However, the methodological weaknesses of some epidemiological studies,

[23] "Mutagenicity" refers to the degree to which an agent increases the frequency of cellular mutation; "cytogenetics" is the study of diseases caused by chromosomal abnormalities.

> including their inability to accurately measure exposure and their small numbers of subjects, render these studies difficult to interpret. In contrast, since animal and cell studies permit researchers to isolate the effects of exposure to a single chemical or to known mixtures, toxicological evidence offers unique information concerning dose–response relationships, mechanisms of action, specificity of response, and other information relevant to the assessment of causation.

Reference Manual on Scientific Evidence at 413-14 (emphasis added, footnotes omitted). This citation makes clear that it can be fair for toxicologists to rely on and critique epidemiological studies, just as the epidemiologists who testified before the Court relied on and critiqued toxicological studies.

The ultimate touchstone governing this Court's analysis is whether Dr. Parent's testimony will assist the trier of fact to understand: (1) abstruse scientific matters; and (2) the strength of the logic and inferences that support medical causation. Dr. Parent's report cites almost 800 journal articles, synthesizing the observations and conclusions they contain into an organized overview of many different aspects of manganese toxicity. The Court is convinced that Dr. Parent may, in fact, assist a jury to understand difficult scientific matters. The Court also concludes that nearly all of the opinions expressed in his report are "based upon sufficient facts or data," and are "the product of reliable principles and methods." Fed. R. Civ. P. 702. For the most part, the Court is also comfortable that Dr. Parent can reliably assist a jury to understand the links in the causation chain – that is, that Dr. Parent "applied the principles and methods reliably to the facts of the case." *Id.*

The Court's overall conclusion in not unqualified, however, because certain of Dr. Parent's opinions stray into areas outside of his expertise. For example, Dr. Parent's explanation that inhalation of manganese in welding fumes is causally related to the development of Parkinson's Disease, in particular, depends to too great an extent on expert opinions of other neurologists and neurotoxicologists; his toxicology and chemistry background does not qualify him to render this opinion himself, and plaintiffs have other expert witnesses who are qualified to so opine. The admissibility of other of sub-parts of Dr.

Parent's opinion under *Daubert* also presents a close question.

In its discretion, the Court concludes it is appropriate to allow Dr. Parent to testify.[24] This conclusion rests, in part, on the Court's confidence – based on its experiences at the *Daubert* hearing and its review of Dr. Parent's deposition – that opposing counsel is highly capable of using cross-examination to reveal any weaknesses in the general causation chain about which Dr. Parent opines. Further, the Court states here its intention to sustain, on *Daubert* grounds, any objections to questions seeking to elicit from Dr. Parent an opinion that welding fume exposure can cause Parkinson's Disease specifically, as opposed to neurological injury generally. While toxicological expertise may require facility with epidemiological research, Dr. Parent tends to opine outside of his area of expertise when he offers overview and discussion of neurological and neuropathological research. *See* footnote 19, above.

With that caveat, the motion to exclude Dr. Parent's opinions based on lack of qualifications is **denied**.

D. Dr. Wells.

Plaintiffs have designated Dr. Martin Wells, who is a statistician, to opine about the strengths and weaknesses of the statistical analyses contained in various epidemiology studies. These studies are all

[24] The Court has struggled somewhat with Dr. Parent's very-wide-ranging declaration. As to certain portions of Dr. Parent's opinions, the question of admissibility is close enough that the Court believes the opposite ruling could also be correct. *See Moore v. Ashland Chemical, Inc.*, 151 F.3d 269, 279 (5th Cir. 1998) (Benavides, J., concurring) ("While I believe this case to be a close one, I must agree that the magistrate judge acted within her discretion in excluding Dr. Jenkins's proffered testimony. It does not follow from this, however, that she would have abused her discretion by admitting the proffered testimony. On the contrary, had she admitted the testimony, I would likewise be of the opinion that she acted within her discretion.").

directed at whether there is an association between welding fume exposure and development of neurological damage. Much of Dr. Wells's attention is directed at the supposed weaknesses of studies cited by the defendants, although he also opines about the supposed strengths of studies cited by the plaintiffs. Dr. Wells also undertakes his own statistical analysis of mortality data collected by the National Center for Health Statistics. Dr. Wells ultimately concludes that all of these materials "do not establish the absence of an association between welding fumes and neurological damage. * * * If anything, the materials may suggest the existence of such an association . . . ." Declaration at 2. During the Court's *Daubert* hearing, the parties examined Dr. Wells extensively about the bases for his opinions.

In their motion, the defendants note that Dr. Wells is "simply a statistician," and not a medical doctor or epidemiologist; that Dr. Wells has no previous experience or training in matters involving welding rods or neurology; and that Dr. Wells has never been published as even a co-author of any epidemiological study. Motion at 1-3. Defendants argue that Dr. Wells's "opinions are nothing more than armchair statistics," and assert that his "lack of understanding and appreciation of medicine leads him to make erroneous statements," such as confusing parkinsonism with Parkinson's Disease. *Id.* at 8. Defendants conclude that, "[n]ot only does Dr. Wells lack that requisite knowledge, skill, experience, training, or education to opine on the issues of epidemiology, welding fumes, and movement disorders, it is clear that he is willing to offer sheer conjecture to bolster plaintiffs' position." *Id.* at 9. Defendants ask the Court to preclude Dr. Wells from testifying about any studies in the epidemiological and scientific literature discussing the existence *vel non* of an association between exposure to welding fumes and neurological damage.

The Court concludes defendants' *Daubert* challenge to Dr. Wells is not well-taken. As to qualifications, Dr. Wells's credentials as a statistician are well-established and beyond reasonable

challenge. For example, he serves as Professor of Clinical Epidemiology and Health Services at Cornell Medical School, and is the chairperson of Cornell's Department of Biological Statistics and Computational Biology. Dr. Wells is a Fellow of the Royal Statistical Society and the American Statistical Association,[25] and was Editor of the latter organization's Journal. He has also published many articles in peer-reviewed journals, including analyses of biological and genetic data. That Dr. Wells is not an epidemiologist is not at all decisive, as his understanding of statistical principles and methodology relevant to the design and interpretation of epidemiological studies is thorough and clear.[26]

Further, Dr. Wells did not attempt to deliver opinions outside the bounds of his expertise, and defendants do not really argue that he did. Most of Dr. Wells's opinions are grounded in observations about various epidemiological studies' confidence intervals, their post-study power, whether they conclusively support the null hypothesis, the propriety of using stepwise regression and one-sided p-values, and so on. All of these opinions are squarely within Dr. Wells's area of expertise. Defendants also mounted attacks on several aspects of the methodologies Dr. Wells used to support certain opinions. The defendants' most colorable arguments regarding Dr. Wells's methodologies were: (1) his use of post-hoc and retrospective power calculations did not accurately reflect the validity of certain epidemiological studies; and (2) his analysis of mortality data from the National Center for Health Statistics ("NCHS") was fatally flawed. The Court concludes, however, that allowing cross-examination to expose any weaknesses in these methodologies is both sufficient and preferable, rather than wholesale exclusion of Dr. Wells's

[25] Only about ⅓ of one percent of the members of the American Statistical Association are recognized as Fellows.

[26] Indeed, calling Dr. Wells "simply a statistician" is both unfair and uninformed.

opinions.[27]

Ultimately the opinions offered by Dr. Wells are relevant to the central epidemiology issues in this case, and Dr. Wells is qualified to offer them. Further, the Court concludes his opinions will be helpful to the jury in understanding the import of the epidemiology studies offered by both plaintiffs and defendants, and in assessing the testimony of other witnesses.[28] Accordingly, the motion to exclude Dr. Wells's opinions based on lack of qualifications is **denied**.

E. Dr. Levy.[29]

Plaintiffs have designated Dr. Barry Levy, who is a medical doctor, epidemiologist, and specialist in Occupational Medicine, to offer testimony about the following subject matters:

a. General descriptions of occupational medicine and epidemiology.
b. The State of the Art over time with respect to what was known or knowable in the

[27] Regarding Dr. Wells's analysis of NCHS data, for example, Dr. Wells did not determine what data would be collected, or how, and he did not collect the data himself; rather, he simply applied statistical analysis to the data after it was gathered. This statistical analysis was within his area of expertise, and did not require additional expertise as an epidemiologist. While defendants labored capably to expose flaws and limitations in Dr. Wells's NCHS data methodology, any such shortcomings were not so grave as to require complete exclusion of Dr. Wells's opinions. Moreover, that Dr. Wells's analysis is not published is not dispositive: "In the absence of independent research or peer review, experts must explain the process by which they reached their conclusions and identify some type of objective source demonstrating their adherence to the scientific method." *In re: PPA Prods. Liab. Litig.*, 289 F.Supp.2d at 1238. This Dr. Wells did.

[28] The Court concludes Dr. Wells's opinions may assist the jury in spite of the oft-repeated indictment that "there are three kinds of lies: lies, damned lies and statistics." (Benjamin Disraeli, quoted by Mark Twain in his Autobiography.) In fact, the parties' discussion of the statistical underpinnings of the many studies cited did help the Court understand the strengths and weaknesses and (most importantly) limitations of those studies.

[29] The Court addresses in this section of the Order only Dr. Levy's opinions regarding the "state of the art of the medical science regarding manganese," which is the subject of defendants' motion at docket no. 972-7. In section III.F of this Order, below, the Court addresses Dr. Levy's opinions regarding business ethics and "prudent practices," which is the subject of defendants' motion at docket no. 972-8.

scientific and medical literature about manganese toxicity, in general, and, in particular, what was known or knowable about welding fume toxicity.

c. What the welding industry and defendants knew or should have known about welding fume toxicity, as evidenced by industry documents, and how industry and defendants' actions (or inactions) measured up to prudent practices of occupational health.

d. General causation, including epidemiology.

Declaration at 4. Dr. Levy's analysis involves an historical review and comparison of, on the one hand, the publicly available medical and scientific literature regarding manganese and welding fumes; and, on the other hand, the defendants' internal documents regarding the same subject. His ultimate conclusions are that: "(1) manganese toxicity has been well established in the scientific and medical literature for many decades; (2) manganese in welding fumes causes brain damage in welders; [and] (3) the welding industry and defendants have been aware of this information for many years and have acted to restrict this information from being disseminated to end-users and others." *Id.* at 13.

Defendants assert that Dr. Levy is "not qualified to present the medical historical testimony he proffers," and also assert that his methodology is not reasonably reliable. Motion at 2. Defendants argue that Dr. Levy has no training as an historian, and no special expertise in the area of neuro-degenerative disorders, so that opinions deriving from his historical review of the public scientific literature and the welding industry's internal documents fall outside of his area of expertise. According to defendants, Dr. Levy merely offers "a narrative of the case which a juror is equally capable of constructing," motion at 8 (quoting *In re Rezulin Prods. Liab. Litig.*, 309 F.Supp.2d 531, 551 (S.D.N.Y. 2004)); defendants go so far as to say that a lay jury "is equally able to read and understand the documents on which Dr. Levy relies." Reply at 5.

The assertion that Dr. Levy is not qualified to testify is easily dismissed. Dr. Levy is board-certified in both internal medicine and also occupational medicine; in addition to being a medical doctor,

he also has a Masters Degree in Public Health from Harvard; he served as a medical epidemiologist with the Centers for Disease Control; and he has authored numerous books and articles within the disciplines of epidemiology and occupational medicine, including a 2003 article reviewing the then-current field of knowledge on occupational exposure to and neurological effects of manganese. He has testified as an expert in other toxic tort cases involving asbestos, silica, benzene, lead, arsenic, hormone therapy, and welding fume exposure. That he is not an expert in neurology or in the field of historical medical documents is not disqualifying in this case, as his combined background in epidemiology and occupational medicine (which is fairly rare) provide sufficient expertise upon which the opinions he offers in his declaration, as a general matter,[30] are properly based.

The Court also disagrees that Dr. Levy's methodology is unreliable. First, it is worth noting that "an expert on the stand may give a dissertation or exposition of scientific or other principles relevant to the case, leaving the trier of fact to apply them to the facts." Fed. R. Evid. 702 (Advisory Committee Notes to 1972 Proposed Rule). Thus, a "narrative" by an expert is not automatically inadmissible; it is only when, as in *In re Rezulin*, the narrative is purely "a repetition of the factual allegations in plaintiffs' complaint," involving "nothing technical or scientific," that a court might find the expert testimony unhelpful, because the expert is providing only "simple inferences drawn from uncomplicated facts." *In re Rezulin*, 309 F.Supp.2d at 551 and n.67.[31] In this case, the great majority of the documents and articles that Dr. Levy is reviewing and comparing are complicated, and the inferences those documents may or

[30] As discussed in the final paragraph of this section of the Order, however, the Court concludes there are certain, specific matters to which an objection at trial would be sustained.

[31] The *Rezulin* court also noted that any "historical commentary of what happened" is "properly presented through percipient witnesses and documentary evidence," not expert narrative. *In re Rezulin*, 309 F.Supp.2d at 551. In this case, there are no percipient witnesses to explain much of the relevant history or to provide historical context to documents.

may not support are not at all simple. It is through the application of his expertise that Dr. Levy may allow the trier of fact to better understand what the documents do (and don't) mean, and, thus, what the defendants did (or didn't) know. It is *not* the case that "the untrained layman [is] qualified to determine intelligently and to the best possible degree the[se] particular issue[s] without enlightenment" from experts. Fed. R. Evid. 702 (Advisory Committee Notes to 1972 Proposed Rule).

It is true that defendants identified possible weaknesses in Dr. Levy's analysis. For example, defendants identified several of what it believes were "remarkable omissions" – relevant historical documents pertaining to manganese exposure that Dr. Levy had not seen. Motion at 7-8. Dr. Levy also freely admitted that his understanding of the differences between various types of related neurological disorders, and his knowledge of the history of certain developments in the field of neurology, was limited. *Id.* at 9-12. The Court concludes, however, that these matters are fodder for cross-examination; they do not so undermine the reliability of Dr. Levy's opinions that a jury should not hear his testimony. Accordingly, the motion to exclude Dr. Levy's opinions is **denied**.

Nonetheless, the Court adds the following caveats. The Court retains some concern that, like Dr. Cunitz, Dr. Levy may be asked to offer testimony that is based largely on personal belief or on his own assessment of the weight of the evidence, and not on a reasoned, independent analysis of the facts. The Court is also concerned that, like Dr. Parent, Dr. Levy may be asked to offer testimony about links in the causation chain that he is not qualified to forge. Particularly, while Dr. Levy's medical expertise is not debatable generally, Dr. Levy has not performed the necessary studies or been involved in development of the medical literature to such a degree that he is qualified to opine that there is a causal neurological link between welding fumes and brain damage in welders. Thus, while Dr. Levy may testify that certain opinions are reflected in the historical medical literature on this issue, he may not pass judgment on the

validity of those opinions or adopt them as his own.

Accordingly, the Court makes clear here that it reserves fully its authority to sustain at trial objections to Dr. Levy's testimony, if it does not strictly adhere to: (1) the *Daubert* standards, (2) the Federal Rules of Evidence, and (3) Dr. Levy's true area of expertise. The Court acknowledges that defendants' motion, though denied, did properly sensitize the Court to evidentiary issues that may remain for trial.

F. Dr. Hoffman.

Plaintiffs have designated Dr. W. Michael Hoffman, who is a Professor of Philosophy and Ethics, to offer testimony about business ethics generally and also whether the defendants acted ethically in this case. Specifically, Dr. Hoffman first sets out the following seven ethical principles, to which, he asserts, all modern businesses should adhere:

1. A corporation should do no unjustifiable harm to its customers, employees, and others affected by its operations. In particular, it should not expose the users of its products to such harm when it knows, or reasonably out to know, that some degree of harm is a likely consequence of ordinary use.

2. A corporation should adopt ethically justifiable values that should inform its policies and culture.

3. A corporation should ensure that its management practices, business decision-making and actions are in accord with ethically justifiable values.

4. A corporation's senior management should set a strong moral tone for the organization and show ethical leadership through words and deeds.

5. A corporation should act with honesty and integrity at all times, telling the truth even when it may not be in its self-interest to do so – this includes the duty to make timely, truthful and complete public communications pertaining to its business and products.

6. A responsible corporation should recognize its role in society and address the impact of its operations on that society through appropriate consultation and communication with government agencies and the public.

7. A corporation should do more than comply with applicable laws and regulations, particularly if circumstances dictate that possible harm could result from a failure to do more.

Declaration at 11-14.

Dr. Hoffman then examines whether the defendants met each of these ethical standards, and opines that they did not. Regarding the second standard, for example, Dr. Hoffman reviewed various written materials and concluded there was "little or no evidence that the Defendants adopted ethically justifiable values which they integrated into their business process." *Id.* at 21. Dr. Hoffman's final conclusion is that "the Defendants have taken a thoroughly reactive approach to safety issues, failing to clear the ethical bar by some margin. There were many missed opportunities to assume voluntary responsibility for promoting the safe use of their products, yet the welding industry as a whole was content to respond only when legislation left no alternative." *Id.* at 29.

Defendants argue that Dr. Hoffman's opinions must be excluded for the following reasons: (1) they are unreliable under *Daubert*, both because the field of business ethics has no standard methodology, and because Dr. Hoffman is insufficiently knowledgeable about the welding industry in particular; and (2) they are unhelpful and confusing to the jury (and even entirely irrelevant), because the *ethical* standards he lists are different from the *legal* standards that apply in this case.[32]

In response, plaintiffs assert that Dr. Hoffman's opinions will "help jurors evaluate Defendants' actions as they relate to Plaintiffs' allegations of conspiracy, fraud, and misrepresentation." Brief in opp.

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[32] Defendants do *not* argue that Dr. Hoffman is unqualified to offer expert testimony in the field of business ethics. In fact, Dr. Hoffman is highly qualified as an expert in his field, having: (1) founded the Ethics Officer Association and the Society for Business Ethics; (2) written 16 books on the subject of business ethics, including some of the earliest, seminal works; and (3) served on the advisory board to the United States Sentencing Commission regarding the role a business ethics program should have in the sentencing process for corporations. Although the Court concludes Dr. Hoffman's opinions are not admissible in this case, the Court can certainly imagine cases where his expertise would be admissible and relevant to the issues raised.

at 10. Plaintiffs explain:

> This litigation deals with the interaction among and between all members of the welding consumable industry [– insurers, trade associations, and manufacturers –] and injuries caused by the acts of these entities. [Most] of the Defendants [are] multinational conglomerate corporations. The average juror may have some knowledge of how the business of a "mom and pop" drug store or supermarket is run, but most will not have any experience or knowledge in relation to such a large scale business and industry. With annual sales in the billions of dollars, most jurors will have no framework for comparing the business methods and practices of Defendants to any of their own experiences. In response to this perceived difficulty, the Plaintiffs anticipate that Dr. Hoffman will be able to simplify somewhat the business methods and practices of Defendants for the jurors and offer an acceptable framework for the jurors to use as they determine whether such conduct was proper. Accordingly, Dr. Hoffman's proposed testimony will be both useful to the jury and will provide the appropriate framework for the jury's deliberations without usurping the jury's function.

Id. at 12-13.[33]

Having weighed the parties' arguments, the Court concludes that defendants have the stronger

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[33] At the *Daubert* hearing, counsel for plaintiffs further argued that Dr. Hoffman's testimony was not problematic merely because it established norms of ethical corporate behavior:

> Now, [defendants] invoke "normative" as a pejorative term, but that is exactly what negligence is. When we have a negligence cause of action, what the conduct of a defendant is measured against is an objective standard. It is the reasonable person. * * * And so by definition, you are comparing the defendants' conduct to some standard, some normative standard.
> * * *
> In this case, the jury is going to be asked to move beyond [a simple automobile accident negligence case] by two steps. They are going to be asked to consider what a reasonable company would do, and not only that, but they are going to be asked to consider and compare the defendants' conduct to what a reasonable manufacturer of welding consumables would do, because [manufacturers] have special knowledge, and I think the standard jury charge instruction will say that a manufacturer is held to an even higher standard than a normal corporation.
> * * *
> [So] what we have in the context of negligence [in this case], Your Honor, is asking the jury to compare defendants' conduct to some standard, this reasonable corporation, this reasonable manufacturer, and * * * an untrained layman needs evidence, information about what the reasonable company, corporation, manufacturer would do.

Transcript at 1530-31 (May 4, 2005).

position. Notably, every one of Dr. Hoffman's seven ethical standards is precatory – each sets out what a corporation *should* do. No right-minded person would disagree with the aspirational character of Dr. Hoffman's ethical principles. But the critical question for the jury in this case is whether the defendant corporations did what the law *required* them to do, not whether, from a societal perspective, they did what an "ethical corporation" *should have* done. Dr. Hoffman's opinions regarding the latter, accordingly, will tend to misdirect the finder of fact.[34]

That Dr. Hoffman's opinions are likely to confuse the jury is highlighted by his seventh ethical principle: "A corporation *should do more than comply with applicable laws and regulations*, particularly if circumstances dictate that possible harm could result from a failure to do more." (Emphasis added.) Simply, Dr. Hoffman sets out a standard in excess of what the law requires; this is unlikely to "assist the trier of fact to understand the evidence or to determine a fact in issue." Fed. R. Civ. P. 702. Further, the Court does not believe that plaintiffs' suggestion of a limiting instruction is workable, given that Dr. Hoffman's measurement of defendants' conduct using "higher-than-legal-standards" weaves through his entire declaration.[35]

As to plaintiffs' concern that lay jurors will be left without guideposts regarding what a "reasonable

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[34] It is also notable that identifying what a corporation or person "should" do is inherently ambiguous when viewed through a legal lens. *See Von Kalinowski v. United States*, 151 Ct. Cl. 172, 1960 WL 8496 at *4 (Ct. Cl. Nov. 2, 1960) ("The word 'should' * * * is a loose and deceptive term. As a breeder of confusion this slippery little word has few peers. The cases disclose its meaning can be, depending on the context of its use, mandatory or directory, imperative or precative, obligatory or discretionary, must or may, and so it goes, a veritable Yin and Yang dichotomy.").

[35] *See e.g.*, declaration at 9 ("Just because a proposed action is legal does not mean it is right or that it conforms to company or social values."); *id.* at 10 ("Business ethics, which is concerned with behaviors, includes and goes beyond legal compliance . . . ."); *id.* at 14 ("If a reasonable consumer would consider that having [certain knowledge about a product] is important, . . . the corporation should reveal that information even if not legally required to do so.").

corporation" is supposed to do under the law, the Court has great confidence in: (1) the jurors' collective knowledge; and also (2) the parties' ability to provide appropriate proposed jury instructions. Regarding the former, jurors decide the vast majority of claims brought against corporations without help from an expert business ethicist, including claims of product liability asserted in federal multi-district litigation. *See In re Rezulin Prods. Liab. Litig.*, 309 F.Supp.2d 531, 542-545 (S.D.N.Y. 2004) (excluding expert testimony on business ethics after agreeing with the defendants that it was: "(1) unreliable because purely speculative; (2) unhelpful to the fact-finder because irrelevant in a case where liability is premised on legal, not ethical, standards, and (3) likely to prejudice and confuse fact-finders concerning the pertinent legal standards"). Regarding the latter, standard jury instructions usually do a fine job of explaining to jurors what duties a reasonable corporation is legally required to undertake. For example, the pattern Ohio Jury Instruction regarding a claim for failure to warn explains:

> One who manufactures a product for sale is held to the skill of an expert in that business and to an expert's knowledge of the arts, materials and processes involved in the development, production and marketing of the product. The manufacturer has the duty to remain reasonably current with scientific knowledge, development, research and discoveries concerning the product. The manufacturer must communicate its superior knowledge to those who, because of their own limited knowledge and information, would otherwise be unable to protect themselves.
>
> However, a manufacturer need not instruct or warn (regarding the use of its product) unless and until the state of medical, scientific and technical research and knowledge has reached a level of development that would make a reasonably prudent manufacturer aware of the unreasonable risks of harm created by the product and aware of the necessity to instruct or warn (ordinary users of the product) against such risks of harm.

3 Ohio Jury Instructions §351.07(2) (2003); *see also In re Joint Eastern and Southern Districts Asbestos Litig.*, 762 F.Supp. 519, 526-27 (E.D.N.Y. 1991) (setting out a jury instruction regarding a manufacturer's duty to investigate the hazards of its product). It is this standard, and not what an ethical corporation "should have done," that matters. Dr. Hoffman's opinions on a corporation's purported ethical requirements, and whether a particular defendant met those requirements, will not help a juror navigate

this instruction; indeed, because his opinions are all premised on a moral compass, not a legal one, confusion is almost assured.

In sum, the Court concludes that Dr. Hoffman may not testify *in plaintiff's case in chief*. The Court holds open the remote possibility, however, that it may allow Dr. Hoffman to testify in rebuttal. Specifically, plaintiffs have suggested that certain defendants may testify that their actions always comported with the highest ethical standards. It is conceivable that the Court might then allow plaintiffs to call Dr. Hoffman on rebuttal to explain: (1) the ethical principles that apply to a business; and (2) whether certain conduct meets these universal ethical standards.[36] With that caveat, the motion to exclude Dr. Hoffman's testimony is **granted**.

For the same reasons, the Court also **grants** the defendants' motion to exclude the "ethics testimony" offered by Dr. Zimmerman and Dr. Levy. In deposition, Dr. Zimmerman opined that: (1) a manufacturer's duty to warn goes "beyond a legal duty; [it is also] a moral obligation;" and (2) a manufacturer has a duty of "product stewardship," which is "more along the lines of a moral obligation." Depo. at 214, 220. This testimony does not survive defendants' challenge under *Daubert*, as plaintiffs conceded at oral argument. Only slightly less objectionable are Dr. Levy's opinions regarding "how industry and defendants' actions (or inactions) measured up to prudent practices of occupational health." Declaration at 4. Dr. Levy explained that, in his opinion, whether a defendant's actions measure up to "prudent practices of occupational health" is measured by whether the defendant complied with the "Precautionary Principle." This principle "call[s] for policies to protect health from potential hazards even

[36] Even within this possibility, the Court is less likely to allow testimony on the second type of explanation, and even then, only in the form of answers to hypothetical questions.

when definitive proof and measurement of those hazards is not yet available."[37] In other words, the duties demanded by this principle are not coterminous with the legal obligations that are relevant in this case, especially because "[r]eversal of the burden of proof is often cited as a corollary to the precautionary principle."[38] Just as Dr. Hoffman's and Dr. Zimmerman's opinions regarding the manufacturers' ethics are insufficiently reliable and likely to confuse the jury, the Court concludes Dr. Levy's opinions about "prudent practices" are inadmissible.

H. Dr. Lees-Haley.

Defendants have designated Dr. Paul Lees-Haley, who is neuropsychologist, to offer testimony about the strengths and weaknesses of various neuropsychological and neurobehavioral testing methods. Defendants' principle purpose for calling Dr. Lees-Haley at trial would be to attack the opinions of plaintiffs' own expert neuropsychologist, Dr. Rosemarie Bowler. While Dr. Bowler opines that exposure to welding fumes causes neuropsychological injury and neurobehavioral deficits, Dr. Lees-Haley's ultimate conclusion is that "Dr. Bowler does not have a scientific basis for the opinions she is offering in her expert report." Declaration at 40.

At the Court's May 2, 2005 *Daubert* hearing, the parties presented argument regarding whether Dr. Lees-Haley was sufficiently qualified to offer the opinions contained in his expert report. Due to

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[37] Frank Ackerman & Lisa Heinzerling, *Priceless: on Knowing the Price of Everything and the Value of Nothing*, SK058 ALI-ABA 571, 574 (ALI-ABA Course of Study, February 16-18, 2005); *see also New Mexico v. General Elec. Co.*, 335 F.Supp.2d 1185, 1221 (D. N.M. 2004) (the Precautionary Principle "requires that in the light of scientific uncertainty, when credible evidence is put forth that a risk exists, action should be taken to minimize that risk or eliminate it even though absolute proof has not been obtained which quantifies the risk.").

[38] Sonia Boutillon, *Book Review*, 16 Eur. J. Int'l L. 164, 164 (Feb. 2005).

timing issues, the parties reserved for the upcoming July 25, 2005 *Daubert* hearing the related questions of: (1) whether Dr. Bowler is sufficiently qualified to offer her own opinions; and (2) whether the methodology underlying both Dr. Lees-Haley's and Dr. Bowler's opinions meet the *Daubert* reliability standard. Subsequently, however, plaintiffs have withdrawn Dr. Bowler as a core expert, thus mooting any immediate need for the Court to rule on the pending motion to exclude the testimony of Dr. Lees-Haley.

If plaintiffs designate other expert neuropsycholgists to testify in future MDL trials, defendants may have reason to call Dr. Lees-Haley. But it is certain that defendants will not call Dr. Lees-Haley at the first MDL trial (*Ruth v. A.O. Smith Corp.*, case no. 04-CV-18912). Accordingly, the Court **denies as moot** the motion to exclude Dr. Lees-Haley, **without prejudice** to plaintiffs' later filing a similar motion, if circumstances warrant.

I. Epilogue.

Although the Court denies most of the parties' motions to exclude various experts, the Court also concludes that these experts will not be without testimonial constraint. The Court has tried to explain, for each expert, where it will set limits and why, but the precise extent that a party will have to rely on cross-examination instead of a sustained objection must be left for trial. The Court is confident that the parties will make every good faith effort to adhere at trial to the limitations the Court has attempted to describe.

The Court also adds that it reserves the right to revisit these rulings as this MDL progresses. The Court may find, for example, that an expert's performance at trial proves the Court's current perception of his qualifications, or the reliability of his methodology, was exaggerated. The Court's duty to admit testimony only if allowed under *Daubert* and the Federal Rules of Evidence is a continuing one.

IV. The "PD Motion."

Defendants have filed what has become known as the "PD Motion" – a motion to exclude all testimony, from any witness, that exposure to welding fumes causes Parkinson's Disease ("PD"). While couched as a *Daubert* motion and filed pursuant to the Court's schedule for the filing of *Daubert* motions, the PD motion really has two distinct elements to it: (1) a fairly typical *Daubert* challenge by which defendants argue that there exists insufficient scientific evidence of "general causation" – that is, evidence of a link between manganese exposure and Parkinson's Disease – to allow expert testimony opining that such a general causal link exists; and (2) a request that the Court rule that, given the lack of reliable evidence of a causal link between manganese exposure and PD, any plaintiff who has PD cannot prevail at trial, as a matter of law, on his claims that his disease was caused by defendants' products.

The briefing connected to this motion has been overwhelming, totaling over 300 pages, with citations to literally hundreds of medical, epidemiological, and scientific articles. At the *Daubert* hearing, both plaintiffs and defendants presented world-class experts in the fields of epidemiology, neuropathology, neuroradiology, and neurology, to explain the most cutting-edge research on the question of whether manganese exposure can cause PD. The Court has been pleased to receive work from both plaintiffs and defendants that is of such high quality. The Court has been privileged, moreover, to have an opportunity to hear from and engage in dialogue with medical professionals possessing such a high caliber of

expertise.[39]

Having worked hard to understand the breadth and depth of the evidence presented by the parties, including reading the scientific articles, expert declarations, and other exhibits provided by the parties, the Court concludes that both aspects of the defendants' PD Motion must be denied. As explained below, however, the Court further concludes that it might still find well-taken, in a particular case, a defense motion for judgment as a matter of law, pursuant to Fed. R. Civ. P. 50 or 56, if the Court is convinced that: (1) given the precise constellation of symptoms and test results presented by a plaintiff, (2) there is no reliable medical or scientific evidence upon which to base a conclusion that, more probably than not, the plaintiff's actual condition was caused by exposure to manganese in welding fumes.

A. Analysis.

It is impossible to fully recapitulate in this Order the nuances of the defendants' many-pronged arguments, or the finer points of plaintiffs' multi-faceted responses; indeed, the volume of evidence presented makes it difficult even to summarize all of each side's strongest points. The discussion below is the Court's attempt to distill to its barest essence the thrust of the parties' positions and the highlights of the Court's conclusions.

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[39] At the *Daubert* hearing, the Court first heard separately from the plaintiffs' and defendants' neurology experts – Dr. Elan Louis and Dr. Warren Olanow, respectively. While both are extremely well-qualified, they expressed dramatically different views regarding whether manganese exposure can cause PD. After receiving this testimony, the Court suggested an additional day of hearings, using what has come to be known as the "hot tub" format: both Dr. Louis and Dr. Olanow would appear before the Court *simultaneously* to answer questions from the Court and to respond directly to each other's opinions. The two experts did re-appear, and the parties and the Court found this "hot tub" approach extremely valuable and enlightening.

1. Parkinsonism.

The defendants begin with the proposition that there are a number of related movement disorders characterized by slow motor function, all of which are classified as "parkinsonisms." All parkinsonisms involve disorders in the area of the brain known as the basal ganglia, which controls voluntary movement and helps establish posture. The classic symptoms common to all parkinsonisms are: (1) "rest tremor," meaning an involuntary quiver of a body part while it is at rest (as opposed to "kinetic tremor," meaning an involuntary quiver of a body part while it is being moved); (2) "bradykinesia," meaning general slowness of movement, including paralysis;[40] (3) "rigidity," meaning stiffness or inflexibility; and (4) "postural instability," meaning loss of normal postural reflexes, and/or a hunched, flexed posture. Persons suffering from a parkinsonism disorder will not necessarily suffer all of these cardinal features, but – by definition – will certainly suffer at least two or more symptoms, with at least one of them being either rest tremor or bradykinesia.

Different forms of parkinsonism may be classified into categories, based on certain common characteristics.[41] For example, "secondary parkinsonisms" are all caused by a known insult to the brain, such as exposure to certain toxic chemicals or drugs (e.g., cyanide, the pesticide Rotenone, or the designer-drug MPTP), head trauma (such as that suffered by Muhammad Ali), certain diseases (e.g., syphilis or encephalitis), or brain tumors. One type of recognized secondary parkinsonism is "manganese-induced

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[40] "Bradykinesia manifests as slowness, such as slower and smaller handwriting, decreased arm swing and leg stride when walking, decreased facial expression, and decreased amplitude of voice." Stanley Fahn, *Description of Parkinson's Disease as a Clinical Syndrome*, 991 Ann. N.Y. Acad. Sci. 1, 6 (2003).

[41] The categories listed here are summarized from Stanley Fahn, *Description of Parkinson's Disease as a Clinical Syndrome*, 991 Ann. N.Y. Acad. Sci. 1, 5 (2003); *see also* Joseph Jankovic, *Parkinsonism*, in CECIL TEXTBOOK OF MEDICINE 2306, 2307 (Goldman and Ausiello, eds., 22nd ed., 2004).

parkinsonism," or "MIP," where the "known insult" to the brain is excessive exposure to and intake of manganese.

Another category is known as "parkinsonism-plus syndromes," which are grouped together because each syndrome is marked by some additional neurological manifestation. For example, persons with progressive supranuclear palsy suffer not only the usual array of movement disorders common to all parkinsonisms, but also an inability to coordinate their eye movements properly; persons with Shy-Drager syndrome suffer the "usual" symptoms and also impairment of their autonomic nervous system, which controls blood pressure, gastro-intestinal motility, and bladder, bowel and sexual functions. A third category of parkinsonisms includes hereditary genetic disorders, such as Wilson's Disease (a genetic inability to excrete copper) and Huntington's Disease (a genetic inability to manufacture certain necessary proteins).

The primary category of parkinsonism, however, is occupied solely by its most common form, which is "simple" PD. Of all persons who suffer from some form of parkinsonism, roughly 60-75% have PD. To a great extent, PD is the diagnosis given to a sufferer of parkinsonism when none of the other disorders fit. That is, an experienced neurologist examining a patient who has the classic parkinsonian symptoms will try to determine whether the patient's disease may be attributed to a genetic cause, such as Wilson's disease, or environmental cause, such as exposure to MPTP, or whether additional symptoms also appear, such as the eye movement disorders associated with progressive supranuclear palsy; finding no such indication, the neurologist will diagnose the patient as having PD. PD is thus sometimes called a "garbage-can" diagnosis, with etiology (or cause) unknown. *See Fahn, supra*, at 8 ("There are no practical diagnostic laboratory tests for PD, and the diagnosis rests on the clinical features and on excluding other causes of parkinsonism."). It is not at all uncommon for persons to be diagnosed as having

PD, and later to be found as having some other form of parkinsonism.[42]

Plaintiffs and their experts agree with these basic principles and distinctions. But plaintiffs and defendants diverge sharply when the discussion turns to the question of whether reliable diagnostic criteria allow doctors to draw definitive and reliable lines between these various disorders.

2. Distinguishing Between Different Forms of Parkinsonism.

The parties do agree that neurologists use four primary tools in their quest to differentiate between the many different forms of parkinsonism that their patients may have: (1) clinical symptoms; (2) levodopa response; (3) neuroimaging; and (4) neuropathology.[43] As explained in section IV.A.3 of this Order, however, while both plaintiffs and defendants agree that neurologists use these four tools, they disagree on which among these tools are most meaningful and on how discriminating each really is.

a. Clinical Symptoms.

The first tool, clinical symptomatology, is simply examination of the visible, physical signs of the disease. As noted above, for example, weakness of eye movements, especially in the downward direction, distinguish progressive supranuclear palsy from PD. One clinical symptom associated strongly with PD and not other parkinsonisms is asymmetrical onset, meaning that the patient's tremor, rigidity, and slowness in limb movement initially manifest on only one side of the body; the other side of the body

[42] *See, e.g.*, www.neurologychannel.com/msa/ ("[Multiple System Atrophy] accounts for about 10% of all cases that are incorrectly identified as Parkinson's [Disease] during life (and upon autopsy are identified as MSA)"); www.psp.org/what_psp.asp ("[Progressive Supranuclear Palsy] is often misdiagnosed as Parkinson's disease because of the general slowing of movement").

[43] A fifth tool, genetic testing, may also be used.

develops symptoms later. Symmetric onset of symptoms suggests a diagnosis of a different form of parkinsonism, and not PD. Similarly, the presence of rest tremor suggests a diagnosis of PD and not some other form of parkinsonism: "although rest tremor may be absent in patients with PD, it is almost always absent in Parkinson-plus syndromes." *Fahn, supra*, at 4-5. Other cardinal clinical symptoms that neurologists look for include the type and speed of the tremor, the type of gait disturbance, and facial presentation (e.g., grimacing appearance versus masked appearance).[44] While defendants characterize clinical symptomatology as only one in this series of essentially equally useful diagnostic tools, plaintiffs argue, and most experts agree, that symptomatology is the most important and most commonly used

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[44] On its website, the American Parkinson Disease Association posts the following description of how a neurologist performs a clinical examination. This description is wholly consistent with the explanations given by both parties' experts:

> Since there is no specific test or marker for PD, diagnosis is by a physician and depends on the presence of at least two of the three major signs: tremor at rest, rigidity, and bradykinesia, as well as the absence of a secondary cause, such as antipsychotic medications or multiple small strokes in the regions of the brain controlling movement. Patients tend to be most aware of tremor and bradykinesia, and less so of rigidity.
>
> To diagnose PD, the physician will perform a standard neurological examination, involving various simple tests of reactions, reflexes, and movements.
>
> - Bradykinesia is tested by determining how quickly the person can tap the finger and thumb together, or tap the foot up and down.
> - Tremor is determined by simple inspection.
> - The physician assesses rigidity by moving the neck, upper limbs, and lower limbs while the patient relaxes, feeling for resistance to movement.
> - Postural instability is tested with the pull test, in which the examiner stands behind the patient and asks the patient to maintain their balance when pulled backwards. The examiner pulls back briskly to assess the patients ability to recover, being careful to prevent the patient from falling.
>
> The examination also involves recording a careful medical history, especially for exposure to medications that can block dopamine function in the brain.
>
> * * *
>
> Several other disorders have certain features that are similar to those of PD, and are sometimes mistaken for PD. These include:
>
> * * *
>
> - Poisoning by carbon monoxide, manganese, or certain pesticides.

www.apdaparkinson.org/APDA/User1/DetailedInfo.aspx?url=Diagnosis.htm

diagnostic tool available to neurologists. *Fahn*, *supra*, at 4-5.

b. Levodopa Response.

The second tool often used by neurologists to differentiate between different forms of parkinsonism is whether the patient responds to therapy using a drug known as levodopa, or "L-dopa." The diagrams below explain, in extremely simplified fashion, how levodopa therapy works. Inside the brain is an area known as the cerebral motor cortex, which governs physical movement; it is from the motor cortex that nerve impulses to the muscles originate. *See* Figures 1 & 2. The motor cortex, in turn, communicates (through feedback loops) with two different brain structures known as the cerebellum and the basal ganglia. The output of the cerebellum is excitatory, while the basal ganglia are inhibitory. The balance between these two systems allows for smooth, coordinated movement, and a disturbance in either system will show up as a movement disorder.

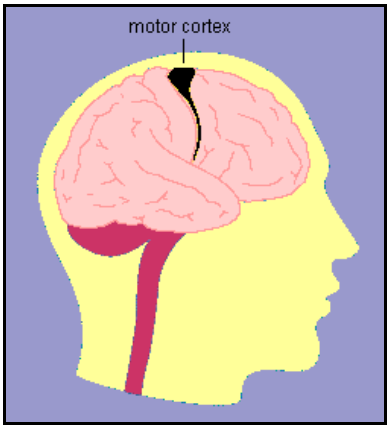

Figure 1

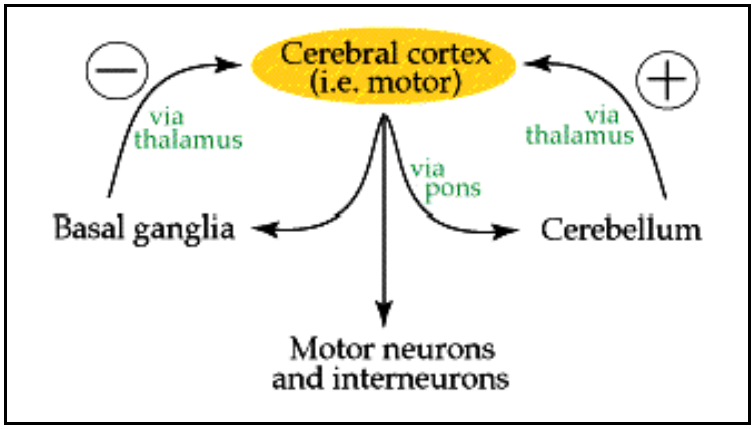

Figure 2

The basal ganglia system, in turn, is made up of a number of structures, including the striatum, the globus pallidus ("GP"), and the substantia nigra pars compacta ("SNpc").[45] *See* Figure 3. Thus, the feedback loop between the basal ganglia and the motor cortex actually involves: (1) neural input from the motor cortex to the striatum; (2) communication between the striatum and globus pallidus; and then (3) neural output from the globus pallidus back to the motor cortex. Meanwhile, the substantia nigra pars compacta communicates with the striatum, using a neurotransmitter called dopamine. The receipt by the striatum of dopamine from the SNpc facilitates the striatum's subsequent communication with the globus pallidus; thus, the SNpc smooths out the entire feedback loop between the motor cortex and the basal ganglia. *See* Figure 4. Damage to any one of the small structures that make up the basal ganglia – the striatum, GP, SNpc, or other areas – will result in a movement disorder.

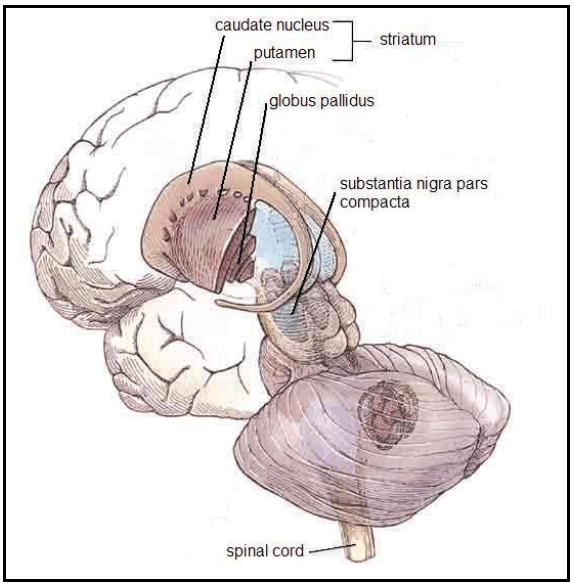

Figure 3

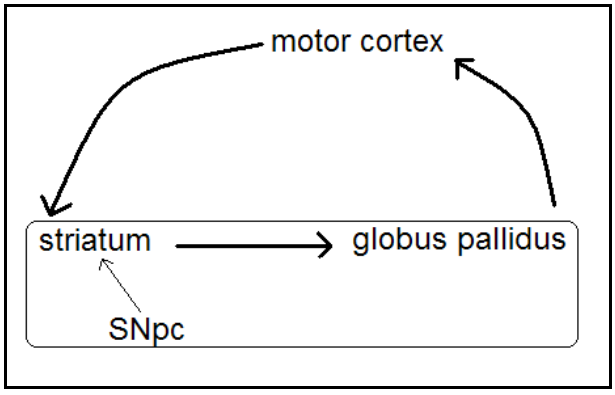

Figure 4

[45] The substantia nigra pars compacta ("SNpc") is geographically close to, but different from, the substantia nigra pars reticulata ("SNpr"); the two structures are both within the basal ganglia but play different roles. Damage to the SNpr does not directly diminish the dopamine production capacity of the SNpc.

The primary form of brain damage that marks a patient who has Parkinson's Disease, in particular, is degeneration of neuronal cells in the SNpc.[46] This damage to the SNpc causes the level of dopamine production in the brain to fall off.[47] Put simply, the SNpc sends inferior amounts of the dopamine neurotransmitter to the striatum, the striatum then communicates poorly with the globus pallidus, the globus pallidus sends inadequate information to the motor cortex, and the motor cortex ultimately fails to send some of the necessary "inhibitory signals" to the patient's muscles. The dearth of these inhibitory muscle signals results in the movement disorders – resting tremor, rigidity, bradykinesia, and postural instability – that are the hallmark of Parkinson's Disease.

The drug levodopa helps to "fix the system" by boosting the dopamine levels in the brain. Once the neuronal cells in the SNpc have died, they are lost forever; however, the drug levodopa is converted inside the brain into dopamine, where it can, once again, facilitate the striatum's communication with the globus pallidus. In essence, levodopa replenishes the dopamine that is no longer manufactured by the damaged SNpc, thereby allowing the entire basal ganglia / motor cortex feedback loop to work properly again. Levodopa sometimes comes with serious side effects, including primarily nausea and dyskinesia,[48] but it can be dramatically effective in alleviating many of the symptoms of Parkinson's Disease.

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[46] As noted below, however, even defendants' own experts agree that some damage to the SNpc can appear in connection with other forms of parkinsonism, and that the SNpc is not the only area of the brain impacted by PD.

[47] A patient does not usually experience the symptoms of PD until roughly 30% or more of the neurons in the SNpc are damaged; until that point, the SNpc still produces enough dopamine for the basal ganglia / motor cortex feedback loop to work smoothly.

[48] "Dyskinesia" is a certain type of involuntary movement, such as a tic or dystonia (a sustained, involuntarily muscle contraction, where the muscle will hold a position). Levodopa-induced dyskinesia, then, replaces the parkinsonian problem of inability to make *voluntary* movements with the "side effect problem" of inability to restrict *involuntary* movements. This side effect usually does not appear until after several years of levodopa therapy.

Levodopa is usually *not* helpful if the damage to the patient's basal ganglia is only to a structure *other than* the SNpc. This is so because, where the SNpc is not damaged, neither is the system's ability to produce the dopamine neurotransmitter. Adding more dopamine to a system already producing a sufficient amount of it generally will not address other defects in the system. Because at least one category of parkinsonisms – the parkinsonism-plus syndromes – is marked by damage to structures of the basal ganglia other than the SNpc, the failure of a patient to respond to levodopa suggests he might suffer from this type of parkinsonism and not PD. *See Fahn, supra*, at 5 ("usually, Parkinson-plus syndromes do not respond to levodopa therapy").[49]

c. Neuroimaging.

The third tool defendants tout as useful in differentiating between different sorts of parkinsonisms is the use of certain neuroimaging techniques, such as positron emission tomography ("PET scans") and single photon emission computed tomography ("SPECT scans"). These tests can measure the neurochemical metabolism and the blood flow in regions of the brain, and can produce both single "snapshots" of the brain and also film-strip-like serial images.[50]

PET scans require the patient to receive an injection of a chemical tagged with a radioactive tracer,

[49] Again, as noted below, even defendants' own experts agree that levodopa responsiveness is not completely definitive. There is clinical evidence that some patients with secondary parkinsonisms respond well to levodopa for at least certain time periods, possibly because flooding an otherwise non-responsive system with excess dopamine may trigger damaged dopamine receptors in the striatum to respond, if only partially or temporarily. Whatever the reason, while levodopa responsiveness may *indicate* the patient has PD and not certain other parkinsonian syndromes, it is by no means determinative in all cases.

[50] Two better-known neuroimaging tests, magnetic resonance imaging ("MRI scans") and computed axial topography ("CAT scans"), are used to evaluate brain *structure* and to produce anatomical images, as opposed to PET and SPECT scans, which measure actual neurochemical *processes* within the brain.

and a scanner can then observe the chemical's actions *in vivo*, or inside the working human body. In the case of neurological testing for parkinsonism, the radioactive chemical is known as fluorodopa, or "F-dopa," which is essentially radioactive levodopa. When levodopa is introduced into the brain, it is absorbed by a specific part of the striatum – specifically, the nigral dopamine terminals in the putamen – and converted into dopamine by an enzyme known as dopa decarboxylase. A PET scan attempts to observe the rate of enzymatic conversion of F-dopa into dopamine inside the putamen. The test thus theoretically allows a radiologist to obtain an index of the amount of damage that has occurred in the SNpc – the lower the rate of enzymatic conversion of F-dopa in the putamen, which is where the SNpc dopamine-producing neurons meet the striatum, the more likely there is damage to the SNpc.[51] Defendants contend that, on a PET scan, the putamen glows brightly in normal patients, while the glow is diminished in patients with PD. Similarly, they assert the putamen also glows brightly on a PET scan of patients who have parkinsonian movement disorders caused by damage to areas of the brain other than the SNpc. In other words, defendants and their experts contend that a PET scan can help differentiate between patients with PD (putamen shows diminished glow) and patients with a different form of parkinsonism (putamen shows normal glow).[52]

Another radiological technique relevant to this case is the magnetic resonance image ("MRI scan"), using a heavily-T1-weighted image contrast setting. This type of MRI scan can reveal where manganese

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[51] A SPECT scan works in similar fashion, using a different radiotracer to measure the level of dopamine enzyme. Currently, however, a PET scan has greater resolution than a SPECT scan, so it is more useful in examining the small areas of the brain involved in parkinsonian disorders.

[52] Plaintiffs' experts challenge the reliability of PET and SPECT scans generally, and specifically assert that "[t]he utility of advanced imaging techniques such as receptor-, transporter-, or enzyme-based in vivo nuclear imaging assays of [dopaminergic] transmission in the diagnosis of parkinsonism due to manganese (Mn) exposure is questionable." Declaration of Martin Pomper at ¶11.

accumulates in the brain. MRI scans of persons with high levels of manganese exposure show deposition of the manganese primarily in the globus pallidus, and not other parts of the basal ganglia.[53] Because deposits of manganese in the brain can clear up over time, an MRI scan will not show manganese deposition several months after the patient's exposure to manganese has ceased.

As discussed below, for a variety of reasons, plaintiffs are skeptical of the usefulness and reliability of these neuroimaging techniques to measure the complex brain functions at the heart of this dispute. This is especially true with respect to PET scans, which plaintiffs' experts assail as exploratory and unreliable.[54]

d. Neuropathology.

The fourth tool neurologists have used to differentiate between different forms of parkinsonism, and upon which defendants place great weight, is neuropathology – the study of brain tissue during a patient's autopsy. The defendants argue that, because different forms of parkinsonism affect different structures of the brain, neuropathology can help distinguish between different syndromes. For example, the defendants contend that the neuropathological pattern in cases of PD is: (1) degeneration of dopamine-producing neurons in the SNpc, coupled with (2) the presence in some of the remaining SNpc neurons of cellular inclusions (protein masses) known as Lewy Bodies, and (3) a lack of substantial damage to the striatum and globus pallidus. In comparison, the neuropathological pattern in cases of progressive supranuclear palsy includes the same degeneration of dopamine-producing neurons in the SNpc that occurs

[53] Radiologists have used MRI scans to examine persons known to have excessive levels of manganese in their blood and urine, including patients whose liver failure prevented the normal excretion of manganese from the body in the bile.

[54] Indeed, this view is apparently not limited to plaintiffs' experts. Most experts, including some designated by defendants as experts in this case, seem to agree that PET imaging should not be used routinely for diagnostic purposes. *See* footnote 67, below.

with PD, but also includes neuronal degeneration in the striatum and globus pallidus (unlike in PD), and the presence of neurofibrillary tangles, rather than Lewy bodies.

Obviously, given that neuropathological examination occurs only after death, it cannot be used to diagnose which form of parkinsonism a living patient has. Neuropathology has recently been used, however, to attempt to make clinical diagnosis more accurate. For example, in a 1992 study by Andrew Hughes, the neuropathological examination of 100 patients, who had been diagnosed during life with PD, showed that 24% had been mis-diagnosed – their brain tissue showed they actually suffered another form of parkinsonism.[55] Hughes then "worked backward," examining the broad array of these parkinsonian patients' clinical symptoms and more carefully correlating each symptom with the now-known neuropathology. Using these more finely calibrated associations of clinical symptoms, correct clinical diagnosis of patients with PD rose to 98%. Hughes was careful to note, however, that these correct diagnoses were made by "experienced fully trained neurologists specializing in movement disorders," and even these specialists had a 15% rate of mis-diagnosis of all parkinsonisms combined.[56]

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[55] Andrew Hughes, *et al.*, *Accuracy of Clinical Diagnosis of Idiopathic Parkinson's Disease: A Clinico-Pathological Study of 100 Cases*, 55 J. of Neurology, Neurosurgery, and Psychiatry 181 (1992). The diagnosing doctors were neurologists and geriatricians; the 24 mis-diagnosed patients actually suffered from progressive supranuclear palsy (6 patients), multiple system atrophy (5 patients), Alzheimer's and Alzheimer's-type disease (6 patients), and a few other parkinsonisms.

[56] Andrew Hughes, *et al.*, *The Accuracy of Diagnosis of Parkinsonian Syndromes in a Specialist Movement Disorder Service,* 125 Brain 861, 868 (2002). In this second study, of the 73 patients whom the specialists gave a clinical diagnosis of PD, 72 were confirmed neuropathologically. On the other hand, neuropathology suggested that another 7 patients had PD, but the specialists had arrived at clinical diagnoses of some other form of parkinsonism. Other mis-diagnoses included diagnosing patients with one type of secondary parkinsonism when they actually had another (e.g., diagnosing a progressive supranuclear palsy patient as having multiple system atrophy). Unfortunately for its usefulness in this MDL proceeding, the Hughes Study did not include any subjects who originally had been diagnosed as suffering from MIP, and apparently did not consider whether any of the patients originally or ultimately diagnosed with PD had a history of exposure to manganese.

3. Parkinson's Disease versus Manganese-Induced Parkinsonism.

The basic premise of defendants' "PD Motion" is that Parkinson's Disease ("PD") and Manganese-Induced Parkinsonism ("MIP")[57] are different entities, and exposure to manganese can cause only the latter. As noted, with their motion defendants argue *both* that: (1) no opinion testimony to the contrary should be admissible, because it is scientifically unreliable; and (2) defendants are entitled to judgment as a matter of law in any case where the plaintiff has PD and not MIP.

In support of their arguments, defendants explain that the four tools discussed above (at least in combination, if not singly) can be used to distinguish between PD and MIP in every case. Discussing these tools in reverse order, the defendants argue as follows.

First, defendants contend the neuropathology of PD is dramatically different from that of MIP. The brain tissue of patients who suffer from PD reveals: (1) significant degeneration of neurons in the SNpc, (2) the presence in some of the remaining SNpc neurons of Lewy Bodies, and (3) a lack of significant damage to the striatum and globus pallidus. In comparison, the brain tissue of patients who suffer parkinsonian symptoms due to severe manganese exposure reveals: (1) a generally-intact SNpc; (2) no Lewy bodies in the SNpc; and (3) significant neurodegeneration in the globus pallidus and also the striatum.

Second, defendants assert that radiological examinations reveal differences in patients suffering PD and MIP. F-dopa PET scans of patients who suffer from PD show a diminished rate of enzymatic

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[57] The scientific literature uses the terms "manganism" and "manganese-induced parkinsonism" interchangeably, although "manganism" sometimes implies more severe, highly-progressed symptoms. *Cf.* Jae-Woo Kim & Yangho Kim, *et al.*, *Three Cases of* ***Manganese Induced Parkinsonism***, 16(3) J. of Korean Neurological Assoc. 336-340 (1998) (emphasis added); Yangho Kim & Jae-Woo Kim, *et al.*, *Positron Emission Tomography (PET) in Differentiating* ***Manganism*** *from Idiopathic Parkinsonism*, 41 J. Occup. Health 91-94 (1999) (emphasis added). The Court prefers the latter term, as it more clearly recognizes that the movement disorder ascribed to manganese exposure is a form of parkinsonism.

conversion of F-dopa in the striatum (the putamen shows diminished glow), while patients with MIP show a normal rate of F-dopa uptake (the putamen shows normal glow). In addition, during and shortly after over-exposure to manganese, a T1-weighted MRI scan will show deposition of the manganese primarily in the globus pallidus, and not in the SNpc. Defendants argue that these different neuroimaging results show that PD is marked by damage to the SNpc, while MIP is marked by damage to other areas of the basal ganglia and not the SNpc.

Third, defendants argue that the response of PD patients to L-dopa therapy is different than the response of MIP patients. PD patients usually experience a strong and sustained, positive response to L-dopa. This beneficial result is so consistent and strong that neurologists use positive L-dopa response as "a well-recognized criterion . . . to distinguish PD from other forms of parkinsonism," such as "striatonigral degeneration, corticobasal ganglionic degeneration, [and] diffuse Lewy body disease." Defendants' reply brief at 36. In comparison, persons suffering from MIP experience, at best, an initial, but weak, positive response to L-dopa therapy, and this positive response subsides relatively quickly. Some MIP patients will experience no positive response to levodopa at all.

And fourth, defendants vigorously contend that the clinical manifestations of PD and MIP are different. Because both PD and MIP are varieties of parkinsonism, they share, by definition, certain symptoms, such as speech disturbance, bradykinesia, postural instability, and rigidity.[58] But, as

[58] Moreover, both PD and MIP patients display a particular type of rigidity – "cog-wheel rigidity" – in the later phases of their diseases. "Cog-wheel rigidity" refers to a muscle that gives way in a series of little jerks upon being passively stretched; neurological examiners feel periodic resistance to the passive movement of a limb. The cog-wheeling is actually a tremor superimposed on a rigid limb – the teeth of the cog are analogous to the tensed parts of the tremor. Neurologists routinely check for cog-wheel rigidity when diagnosing a patient with a parkinsonian syndrome.

summarized in the following table, defendants argue there are other physical symptoms the two syndromes do not share, which can be used to differentiate them.

Symptom – Clinical Manifestation	Parkinson's Disease	Manganese-Induced Parkinsonism
Tremor	Patients almost always present with a tremor. The tremor occurs when the limb is at rest.	Patients sometimes present with no tremor. If tremor does occur, it is often a lower amplitude kinetic tremor (appearing when movement of the limb is initiated), and not a resting tremor.
Symmetry	Patients usually present with asymmetrical symptoms – e.g., tremor on the right side and not on the left – especially at initial onset of the disease.	Patients usually present with symmetrical symptoms.
Facial Presentation	Patients' faces appear expressionless, as though they are wearing a mask; blinking is often decreased.	Patients present with a grimacing appearance.
Gait Dysfunction	Patients have decreased arm swing and leg stride, progressing to the "freezing phenomenon," where the feet are temporarily glued to the ground. Gait abnormality and postural instability appear later in the disease process.	Patients suffer "coq-au-pied," or cock walk, meaning jerky walking on tiptoe, and tend to fall backwards. Gait abnormality and postural instability appear relatively early in the disease process.

Defendants explain that the differences between PD and MIP revealed by these four tools are all related: manganese overexposure damages a different part of the brain than does PD, and these different patterns of damage: (1) appear different radiologically, (2) respond differently to levodopa therapy, and (3) cause different constellations of clinical symptoms. Given all of these differences, defendants conclude, the Court should not allow any expert to opine that exposure to manganese can cause PD, and

should not allow any plaintiff who has been diagnosed as having PD, as opposed to MIP, to prevail at trial. At best, defendants assert, plaintiffs can validly claim, and their experts can legitimately opine, only that exposure to manganese can cause MIP, which is a distinct and different disease.[59]

The Court concludes, however, that it cannot issue the rulings defendants request. The Court concludes both that: (1) there is sufficient scientific data to support the contrary opinions plaintiffs' experts espouse regarding the interplay between manganese exposure, PD and MIP; and (2) judgments regarding a particular plaintiff's condition, and the strength of the parties' scientific evidence of the cause of that condition, must be left for the trier of fact.

Addressing the second of these conclusions first, the Court finds that the scientific evidence defendants use to delimit and define PD is not as "neat" as defendants try to portray it, and that the distinction between PD and MIP is not as clear as defendants paint it. When assessing the strength of this evidence, the Court starts with the tool most often used by practicing neurologists to make differential diagnoses between the two syndromes: clinical symptomatology.

As an initial matter, the Court observes that the neurological community continues to make efforts to more accurately identify individual parkinsonisms by reference to particular constellations of clinical manifestations. For example, Hughes's attempt to "look backward" and better correlate specific groups of symptoms to a certain type of parkinsonism was published only three years ago, in 2002. Shortly before that, a research paper (cited by defendants) was published "to propose diagnostic criteria that reliably distinguish PD from other conditions with parkinsonian features," noting that improved criteria were necessary because "only about 75% of clinical diagnoses of PD are confirmed at autopsy, largely because

[59] As will be addressed in a later opinion, defendants have also filed a separate motion (docket no. 972) arguing there is no scientific evidence to support the opinion that exposure to welding fumes can cause any neurologic disorder, even MIP.

the cardinal signs can also occur in conditions other than PD." Douglas Gelb, *et al., Diagnostic Criteria for Parkinson Disease*, 56 Archives of Neurology 33, 33 (1999).[60] In other words, recent articles in the field recognize that clinical differentiation between PD and other parkinsonisms is currently not so accurate or mature that PD and MIP can be reliably diagnosed or differentiated every time.

It is not that these efforts at more accurate clinical diagnosis cannot be, or are not sometimes (even usually), successful; the point is that, for a number of reasons, these diagnoses are not always accurate. First, it is true that many patients with movement disorders are diagnosed today by doctors who are not well-versed in the diagnostic criteria that the parties' experts discuss. Many clinical textbooks today continue to define PD using highly inclusive definitions.[61] Indeed, some textbooks knowingly *reject* a more precise clinical definition.[62] Put simply: because clinical symptoms of PD and MIP overlap, doctors

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[60] *See also* Ryan Uitti, *et al., Is the Neuropathological 'Gold Standard' Diagnosis Dead? Implications of Clinicopathological Findings in an Autosomal Dominant Neurodegenerative Disorder*, in 10 PARKINSONISM & RELATED DISORDERS 461, 462 (2004) ("The clinical diagnosis is 'incorrect,' with a different neuropathological diagnosis, in approximately one in five patients thought to have Parkinson's disease by an experienced clinician.").

[61] *See, e.g.*, Ali Rajput, *Parkinsonism, Aging, and Gait Apraxia*, in PARKINSONIAN SYNDROMES 511, 514 (Stern & Koller, eds. 1993) ("The diagnosis of [parkinsonian syndrome and Parkinson's Disease] is usually based on the presence of two of the following: bradykinesia, rigidity, and resting tremor. The postural instability may be an early feature or the first manifestation in some cases. Therefore, it has been suggested that two of the following – bradykinesia, rigidity, resting tremor, and postural instability – are sufficient for the diagnosis."). *See also* Pramod Kr. Pal, *et al., Cardinal Features of Early Parkinson's Disease*, in PARKINSON'S DISEASE: DIAGNOSIS AND CLINICAL MANAGEMENT 41, 46 (Factor & Weiner eds. 2002) (Table 6-3 lists 22 different clinical symptoms that can be used to make a differential diagnosis between 10 varieties of parkinsonism. PD is marked most obviously by resting tremor, rigidity, bradykinesia, and asymmetry at onset, plus the lack of other symptoms. MIP is *not listed* in the Table as an option for differential diagnosis, although it is discussed at p. 49.)

[62] *See* Henry Paulson & Matthew Stern, *Clinical Manifestations of Parkinson's Disease*, in MOVEMENT DISORDERS: NEUROLOGICAL PRINCIPLES AND PRACTICES 183 (Watts & Koller eds. 1997) ("Because of the broad phenotypic variability in PD, the lack of a precise and rigid clinical definition may be inevitable and, perhaps, even appropriate. A definition relying too heavily on any one clinical feature runs the risk of excluding legitimate cases.")

using valid clinical definitions of PD will sometimes "correctly" diagnose MIP as PD. That is, a person suffering from MIP will sometimes fit within the clinical definition of PD.

Furthermore, even these cutting-edge efforts at improving clinical diagnostic accuracy are far from foolproof. The plasticity of the brain and the non-linear response of different persons to the same etiological agent means that even the best neurologists using the latest diagnostic criteria will sometimes confuse and mis-diagnose persons with PD and MIP. Dr. Gelb recognized this in his own proposal to improve diagnostic quality: "Criteria based on combinations of clinical features improve diagnostic accuracy, but no criteria proposed to date have achieved a high enough positive predictive value to eliminate the need for autopsy confirmation." Gelb, *supra*, at 36. This is especially true because all parkinsonian movement disorders are *progressive*, meaning they worsen and change over time. Dr. Gelb continues:

> [D]iagnostic confusion is greatest early in the clinical course when some of the more distinctive clinical features may not yet have developed. Thus, to increase specificity, the clinical diagnosis of PD should be regarded as preliminary until parkinsonian symptoms have been present for a substantial period of time to ensure that patients do not develop features suggestive of alternative diagnoses.

Id.

Indeed, one of the problems with defendants' symptom chart on page 59, above, is that many of the clinical manifestations described in the MIP column refer to patients who: (1) suffered extreme overexposure to manganese, as opposed to lower levels of overexposure; and (2) were relatively farther along in their disease progression. To a lesser extent, the PD column also lists symptoms of a patient whose disease has progressed. This works to highlight the clinical differences between the two diseases; to the extent they are clinically distinguishable, the distinction is most accurately made only after the diseases have fully flowered. The fact is that some patients known to have PD do not present with a rest

tremor; and some patients known to have MIP present with a masked face, resting tremor, and asymmetry.[63] There is no question but that patients with MIP have been, and are today being, diagnosed as having PD, for the simple reason that the clinical diagnostic criteria overlap. And, for the same reason, there is also no question but that patients who have "simple" PD – perhaps even patients who are plaintiffs in this case – are being diagnosed today as having MIP.

Adding the other three tools to the analysis does not change the result. Some PD patients do not experience a "strong and sustained" response to levodopa therapy, while some MIP patients do.[64] Indeed, the drug literature states that levodopa is "indicated in the treatment of the symptoms of idiopathic Parkinson's disease (paralysis agitans), post-encephalitic parkinsonism, and symptomatic parkinsonism which may follow injury to the nervous system by carbon monoxide intoxication *and/or manganese intoxication*."[65] Neuroimaging may eventually prove extremely helpful in determining whether a patient has suffered excessive manganese exposure, and in defining precisely the extent and location of neuronal

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[63] *See* Fahn, *supra,* at 4-5 ("rest tremor may be absent in patients with PD"); Jae-Woo Kim & Yangho Kim, *et al.*, *Three Cases of Manganese Induced Parkinsonism*, 16(3) J. of Korean Neurological Assoc. 336-40 (1998) (describing "case one" as first experiencing "a tremor in his right hand," later showing "an expressionless face," with tremors in "his hands and feet when in a settled position, which were especially prominent on his left side," and eventually developing the "cock-walk" distinctive to MIP patients).

[64] *See* C. Warren Olanow, *et al., An Algorithm (Decision Tree) for the Management of Parkinson's Disease (2001): Treatment Guidelines*, 56 Neurology (Supp. 5) S1, S2 (2001) ("Some clinicians have used a 'levodopa challenge test' in attempts to differentiate PD from atypical parkinsonism. This is not particularly helpful because PD patients with very mild features may not show great benefit from levodopa, and patients with atypical parkinsonism may show some benefit, particularly in the early stages of the disease. * * * [A] consensus panel of PD experts has recommended against using this procedure as a diagnostic test."); Shuichirou Nagatomo, *et al, Manganese Intoxication During Total Parenteral Nutrition: Report of Two Cases and Review of the Literature*, 162 J. of the Neurological Sciences 102, 104 Table 1 (1999) (reviewing the literature of MIP patients who were helped by levodopa).

[65] Merck & Co., "indications and usage" for its drug Sinemet, which is a carbidopa-levodopa combination and one of the most commonly prescribed drugs for parkinsonian patients (emphasis added).

damage, as well as in identifying the form of parkinsonism that a patient is suffering. But these radiological tests are currently research tools, not diagnostic tools.[66] Doctors examining parkinsonian patients today are simply not using these radiological tests for differential diagnosis, and the most recent scientific literature counsels against it.[67] Finally, neuropathology is not at all useful to a doctor attempting differential diagnosis of a patient's parkinsonian symptoms, because examination of the patient's brain tissue necessarily occurs posthumously; neuropathology can only *confirm or contradict* a clinical diagnosis after the patient has died. It is also important to note that there are only 14 reported neuropathological examinations of MIP patients, suggesting caution about the accuracy of defendants' generalization regarding differences between MIP and PD brain tissue damage. Again, the most recent scientific literature echoes this need for caution and tends to undermine defendants' assertion that differential

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[66] *See* Richard Dewey, Jr., *Clinical Features of Parkinson's Disease*, in PARKINSON'S DISEASE AND MOVEMENT DISORDERS: DIAGNOSIS AND TREATMENT FOR THE PRACTICING PHYSICIAN 71, 84 (2000) ("Because [F-dopa] has a very short half-life (less than 2 hours), the compound must be synthesized on-site, a requirement that limits this technique to only a few research centers."); Darin Dougherty *et al.*, *Functional Neuroimaging*, in 1 NEUROLOGY IN CLINICAL PRACTICE: THE NEUROLOGICAL DISORDERS 667, 672 (4th ed. 2004) ("The clinical use of [PET scans and SPECT scans as diagnostic tools] is just beginning to emerge.").

[67] *See* Bernard Ravina, *et al.*, *The Role of Radiotracer Imaging in Parkinson's Disease*, 64 Neurology 208 (2005). Dr. Ravina writes, in the article's abstract: "Biomarkers used as diagnostic tests . . . must not only have biologic relevance but also a strong linkage to the clinical outcome of interest. No radiotracers fulfill these criteria, and current evidence does not support the use of [neuro-]imaging as a diagnostic tool in clinical practice or as a surrogate endpoint in clinical trials." *Id.* Regarding four varieties of PET and SPECT scans in particular, Dr. Ravina adds: "None of these techniques reliably distinguishes idiopathic PD from multiple system atrophy (MSA) or other forms of atypical PD. * * * Although there is increasing use of diagnostic imaging by investigators, currently it is not recommended that [dopamine transporter markers] and other tracers be used routinely in the diagnosis of PD or other parkinsonian syndromes." *Id.* at 211.

neuropathology is always reliable.[68] Even defendants concede that MIP patients suffer some damage to the SNpc, and PD patients suffer some damage to the globus pallidus and striatum; at best, the two syndromes are neuropathologically differentiated by where the damage is greatest.

This is not to say that the sum of the data provided by clinical, pharmacological, radiological, and neuropathological testing is of no use in determining whether a particular patient is suffering from MIP, or instead some other form of parkinsonism; far from it. It may well be that, in a particular case, given

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[68] Dr. Gelb, for example, concludes that "there are no universally accepted histopathologic criteria for the diagnosis of PD," and explains this conclusion as follows:

> The absence of a completely reliable *clinical* marker for PD makes *neuropathological* confirmation essential in evaluating the diagnostic utility of clinical features or combinations of features. Classically, the neuropathological features of PD are relatively straightforward: the substantia nigra reveals neuronal loss and Lewy bodies. * * * In patients with typical clinical features and these pathologic findings, the diagnosis is clear.
>
> The neuropathologic findings are sometimes ambiguous or conflicting, however, and the specificity and sensitivity of individual pathologic features are not known. For example, some [PD] patients have typical clinical features and neuronal loss in the substantia nigra, but no Lewy bodies. Conversely, some [PD] patients have Lewy bodies without neuronal degeneration or even clinical abnormalities.

Douglas J. Gelb, *et al.*, *Diagnostic Criteria for Parkinson Disease*, 56 Archives of Neurology 33, 36-37 (1999) (emphasis added).

Even more recently, Dr. Uitti, a researcher at the Mayo Clinic College of Medicine, asserts that confirmation or contradiction of a differential diagnosis of a parkinsonian syndrome using neuropathology alone should be eschewed:

> Just as there is no clinical 'gold standard' for Parkinson's disease, we conclude there is no pathological 'gold standard.' Diagnosis must be based upon patterns of findings, and the task facing both clinicians and pathologist is the assignment of 'weighting' to the individual clinical (e.g. resting tremor) and pathological (e.g. Lewy body) features. * * *
>
> Our observations and arguments also place under scrutiny the practice of defining diseases by clinical or pathological criteria. Instead, we suggest that etiology should be the determining factor in distinguishing separate disease entities. Where we do not know etiology, we can only speak of syndromes."

Ryan Uitti, *et al., Is the Neuropathological 'Gold Standard' Diagnosis Dead? Implications of Clinicopathological Findings in an Autosomal Dominant Neurodegenerative Disorder*, 10 PARKINSONISM & RELATED DISORDERS 461, 463 (2004). *See also* Donald Calne, *et al., The Neuromythology of Parkinson's Disease*, 10 Parkinson and Related Disorders 319, 320 (2004) ("the presence of Lewy bodies in the substantia nigra is neither a necessary nor a sufficient criterion for making a diagnosis of Parkinson's Disease").

the precise constellation and progression of the plaintiff's clinical symptoms, combined with his particular drug responses, test results, work history, family history, age, and so on, there is no reliable medical or scientific evidence upon which to base conclusions that, more probably than not: (1) the plaintiff is suffering MIP instead of "cryptogenic" PD; or (2) his condition was caused by exposure to manganese in welding fumes.

But the defendants are asking the Court to disallow *any* argument or testimony in *any* MDL case that a person diagnosed with PD is suffering because of exposure to manganese in welding fumes. The foundation for such an Order can only be as strong as the accuracy of differential diagnosis between MIP and PD.[69] As explained above, MIP and PD are not so clearly and easily distinguished that a diagnosis of PD definitely means the patient is not actually suffering from MIP. Indeed, PD is often referred to as "idiopathic parkinsonism," meaning its cause is unknown;[70] this is why PD is sometimes called a "garbage-can" diagnosis.[71] A doctor may choose a diagnosis of PD instead of MIP based solely on his failure to ask the patient about manganese exposure, or his failure to know that the question is relevant at all.

Finally, defendants suggest that the Court could still grant their motion, but allow a plaintiff to

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[69] For a good discussion of the medico-legal concept of differential diagnosis, see *Bitler v. A.O. Smith Corp.*, 400 F.3d 1227, 1223-25 (10th Cir. 2004) (petition for certiorari pending).

[70] *See. e.g.,* Pramod Kr. Pal, *et al., Cardinal Features of Early Parkinson's Disease*, in PARKINSON'S DISEASE: DIAGNOSIS AND CLINICAL MANAGEMENT 41, 42 (Factor & Weiner eds. 2002) (referring to "Idiopathic Parkinsonism (commonly known as Parkinson's Disease)").

[71] *See* Donald Calne, *et al., The Neuromythology of Parkinson's Disease*, 10 Parkinson and Related Disorders 319, 321 (2004) ("Instead of looking at Parkinson's Disease as a single disease, we can regard it as a syndrome with many causes, that may be genetic or environmental."); Pramod Kr. Pal, *et al., Cardinal Features of Early Parkinson's Disease*, in PARKINSON'S DISEASE: DIAGNOSIS AND CLINICAL MANAGEMENT 41, 41 (Factor & Weiner eds. 2002) ("it is doubtful whether 'Parkinson's disease' is a single entity").

argue mis-diagnosis. The problem with this suggestion, as noted above, is that, because clinical symptoms of PD and MIP overlap, doctors using *valid clinical definitions of PD* will sometimes diagnose MIP as PD; a person suffering from MIP will sometimes fit within the clinical definition of PD. Thus, it would not be entirely correct to put a plaintiff, who was diagnosed as having PD but who actually suffers MIP, in the position of having to argue he was "mis-diagnosed;" rather, his doctor may have simply and validly chosen one of two overlapping diagnoses. The parties are equally able to argue whether the one chosen was correct.

In sum, an exhaustive review of the science reveals that the defendants' model for differential diagnoses of the various forms of parkinsonism is, indeed, a useful and, at times, definitive tool for distinguishing one parkinsonian movement disorder from another. It is also a model which finds substantial support in the literature and from some of the most respected professionals in the field. Ultimately, however, it is too "neat." Even defendants' own experts recognize that these diagnostic criteria and the tools used to apply them are imperfect – they are guides to diagnosis, but do not guarantee a correct diagnosis in a given case.[72] The Court, accordingly, declines to issue a ruling elevating these diagnostic criteria from useful tools to rigid legal barriers.

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[72] Even the most experienced experts have difficulty "making a call" regarding an appropriate diagnosis in individual cases. In assessing plaintiff Charles Ruth – whose treating physicians have diagnosed him as suffering from MIP based on: (1) a known history of exposure to manganese, (2) a T-1 weighted MRI showing manganese deposition in the globus pallidus, (3) little or no response to levodopa, and (4) clinical symptoms including cock-walk and cogwheel rigidity, *see* Ahmed Sadek, *et al.*, *Parkinsonism Due to Manganism in a Welder*," 22 Int. J. Toxicol., 393, 393 (2003) – defense expert Dr. Warren Olanow was not prepared to agree that Ruth suffers from MIP, as opposed to some other form of parkinsonism, *see* hearing tr. at 1977-78 (he "probably does not" have manganism). *See also* Yangho Kim & Jae-Woo Kim, *et al.*, *Positron Emission Tomography (PET) in Differentiating Manganism from Idiopathic Parkinsonism*, 41 J. Occup. Health 91-94 (1999) ("[i]t is difficult to distinguish manganism and idiopathic parkinsonism from each other").

4. Epidemiology.

In the portion of their papers that does raise a quintessential *Daubert* challenge to the plaintiffs' evidence, defendants focus on the question of "general causation." Defendants move away from their discussion of how diagnostic criteria should be applied to any given patient, and argue that plaintiffs cannot meet the threshold requirement of establishing, through reliable scientific evidence, that exposure to manganese at *any* level causes, contributes to, or accelerates the onset of PD in *any* patient.

The question of whether exposure to manganese caused (or contributed to, or accelerated the onset of) a *particular* plaintiff's parkinsonian syndrome is a question of "specific causation" – did manganese in welding fumes cause the plaintiff's malady, or did some other agent (known or unknown) cause his malady? "Specific causation" addresses "[w]hether exposure to an agent was responsible for a given individual's disease." *Reference Manual on Scientific Evidence* at 396.

A related concept is "general causation," which "is concerned with whether an agent increases the incidence of disease in a group and not whether the agent caused any given individual's disease." *Id.* at 392. In other words, general causation asks if a toxin *can* cause *a* plaintiff's harm; specific causation asks if the toxin *did* cause *the* plaintiff's harm.[73] The inter-relationship between these two concepts, in the context of a *Daubert* analysis, was explained in *Cavallo v. Star Enterprise*:[74]

> The process of differential diagnosis is undoubtedly important to the question of "specific causation". If other possible causes of an injury cannot be ruled out, or at least the

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[73] *See also Reference Manual on Scientific Evidence* at 444 ("General causation is established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance *can* cause a particular disease (e.g., that smoking cigarettes can cause lung cancer). Specific, or individual, causation, however, is established by demonstrating that a given exposure is the cause of an individual's disease (e.g., that a specific plaintiff's lung cancer *was* caused by his smoking).") (emphasis added).

[74] *Cavallo v. Star Enterprise*, 892 F. Supp. 756 (E.D. Va. 1995), *affirmed in relevant part*, 100 F.3d 1150, 1159 (4th Cir. 1996), *cert. denied*, 522 U.S. 1044 (1998).

> probability of their contribution to causation minimized, then the "more likely than not" threshold for proving causation may not be met. But, it is also important to recognize that a fundamental assumption underlying this method is that the final, suspected "cause" remaining after this process of elimination must actually be capable of causing the injury. That is, the expert must "rule in" the suspected cause as well as "rule out" other possible causes. And, of course, expert opinion on this issue of "general causation" must be derived from a scientifically valid methodology.

Cavallo, 892 F. Supp. at 771 (footnote omitted).

One way – but not the only way – of proving general causation is with the use of epidemiological studies. "Epidemiological evidence identifies agents that are associated with an increased risk of disease in groups of individuals, quantifies the excess disease that is associated with an agent, and provides a profile of a type of individual who is likely to contract a disease after being exposed to an agent." *Reference Manual on Scientific Evidence* at 335-36. A renowned example is the 1956 epidemiological study which "showed that smokers who smoked ten to twenty cigarettes a day had a lung cancer mortality rate that was about ten times higher than that for nonsmokers." *Id.* at 336. This early study, however, identified only an *association* between smoking cigarettes and death from lung cancer; it did not show that smoking can *cause* lung cancer, a matter that was proved through additional studies.[75]

In this case, defendants assert that: (1) plaintiffs have not produced reliable epidemiological studies supporting the proposition that exposure to manganese in welding fumes can generally cause, contribute to, or accelerate onset of PD; and (2) there are reliable epidemiological studies supporting the proposition that exposure to manganese in welding fumes does *not* generally cause, contribute to, or accelerate onset

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[75] One of the authors of the 1956 smoking study was A. Bradford Hill, who is well-known for having first codified the factors that guide epidemiologists in making judgments about whether a cause-effect relationship may be inferred from an association. *Reference Manual on Scientific Evidence* at 376 (citing A. Bradford Hill, *The Environment and Disease: Association or Causation?*, 58 Proc. Royal Soc'y Med. 295 (1965)). As noted above, much of Dr. Parent's expert report is devoted to examination of these "Bradford Hill factors."

of PD. The plaintiffs respond that: (1) defendants are wrong, as there are reliable epidemiological studies supporting general causation; (2) defendants' epidemiological studies supporting no general causation are unreliable; and (3) in fact, they do not even need any epidemiological studies, at all, to show general causation.

Between these two positions, the parties have spent an extraordinary amount of time and effort to examine in great detail the strengths and weaknesses of dozens of studies. As the Federal Judicial Center's *Reference Manual on Scientific Evidence* makes clear, "[i]t is important to emphasize that most [epidemiological] studies have flaws. Some flaws are inevitable given the limits of technology and resources. In evaluating epidemiologic evidence, the key questions, then, are the extent to which a study's flaws compromise its findings and whether the effect of the flaws can be assessed and taken into account in making inferences." *Reference Manual on Scientific Evidence* at 337 (footnote omitted). Given that no epidemiological study is flawless, "in most cases, objections to the inadequacies of a study are more appropriately considered an objection going to the weight of the evidence rather than its admissibility. Vigorous cross-examination of a study's inadequacies allows the jury to appropriately weigh the alleged defects and reduces the possibility of prejudice." *Hemmings v. Tidyman's Inc.*, 285 F.3d 1174, 1188 (9th Cir. 2002) *cert. denied*, 537 U.S. 1110 (2003) (citations omitted).

The parties have certainly shown that none of the "epi-studies" presented by either side is perfect. A representative sample of the parties' arguments and rejoinders regarding just a few of the studies cited is set out in the table on the following pages.

Epi-Study	Summary of Study Results	Arguments
Joseph Tsui, *et al., Occupational Risk Factors in Parkinson's Disease*, 90(5) Canadian J. of Public Health 334 (1999).	This study examined current occupations of 7,073 people from Vancouver, Canada – 414 of whom had PD. The study found that teachers and medical workers had an elevated risk of suffering PD, while homemakers and construction workers had a lower risk; welders are not reported as having a lower or higher risk.	Defendants argue this large case-control study shows welders are not at increased risk of suffering PD. Plaintiffs present data suggesting the study included few welders, so no association could have been found; thus, the lack of a reported association carries no meaning. Plaintiffs also criticize the method of determining "occupation."
Caroline Tanner, *et al., Occupation and Risk of Parkinson's Disease (PD): A Preliminary Investigation of Standard Occupational Codes (SOC) in Twins Discordant for Disease* (Abstract S49.001).	This study examined occupational history of 96 pairs of WWII veteran twins (192 people total), where one twin had PD and the other did not. Eight individuals were welders. Overall, no occupation was significantly associated with PD risk; however, examining only identical twins (not fraternal), teachers and healthcare workers had an elevated risk, while welders did not.	Defendants argue this study shows welders are not at increased risk of suffering PD. Plaintiffs argue the study was "under-powered," meaning it was not large enough to ferret out an elevated PD risk to welders, even if one exists – it had only a 13% chance of detecting a statistically significant association.[76]
Jon Fryzek, *et al., A Cohort Study of Parkinson's Disease and other Neurodegenerative Disorders*, 47(5) J. of Occupational & Environmental Medicine 466 (May 2005).	This study examined hospitalization rates due to PD & parkinsonism for 27,839 men, including 6,163 welders. There was no statistically significant difference of hospitalization rates between welders and the general population.	Defendants argue this large study shows definitively that welders are not at increased risk of suffering PD. Plaintiffs argue the study was skewed because, as the study admits, shipyard welders were purposefully excluded, thus omitting those welders with highest fume exposure, who were most likely to suffer PD. Plaintiffs also argue that PD hospitalization rates are not a good measure of actual PD frequency.

[76] Plaintiffs argue that virtually every study cited by defendants is substantially "under-powered." As explained by the *Reference Manual on Scientific Evidence* at 336, "[w]hen a study fails to find a statistically significant association, an important question is whether the result tends to exonerate the agent's toxicity or is essentially inconclusive with regard to toxicity," due to lack of sufficient statistical power. Reciting the refrain that "the *absence of evidence* of a welding/PD association is not *evidence of absence* of such an association," plaintiffs argue that all of defendants' studies finding no association are under-powered, and thus simply inconclusive. Defendants sometimes use the same argument in reverse, asserting that a study suggesting an association between welding and PD includes too little data to be reliable, and is merely reporting an artifact.

Epi-Study	Summary of Study Results	Arguments
David Coggon, *et al., Occupational Mortality of Men,* in OCCUPATIONAL HEALTH DECENNIAL SUPPLEMENT (1995).	This study examined causes of death in British men between 1979 and 1990, categorized by occupation. Welders suffered higher-than-average mortality rates due to pneumonia, but not due to PD.	Defendants argue this study shows welders are not at increased risk of suffering PD. Plaintiffs argue mortality rate studies are generally unhelpful, because PD is rarely listed as a cause of death for persons who have PD. Plaintiffs also assert that the high rate of early pneumonia mortality in welders worked to under-report PD prevalence.
Jay Gorell, *et al., Occupational Exposure to Manganese, Copper, Lead, Iron, Mercury, and Zinc and the Risk of Parkinson's Disease,* 20 Neuro-Toxicology 239 (1999). Jay Gorell, *et al., Multiple Risk Factors for Parkinson's Disease,* 217 J. of Neurological Sciences 169 (2004).	The 1999 case-control study examined 608 people, 144 of whom had PD, for historical occupational exposure to various industrial metals. The study found that: (1) the likelihood of suffering PD did not increase with less than 20 years exposure to any metal; but (2) 20 years or more exposure to manganese increased the likelihood of suffering PD tenfold. The 2004 study then examined the same data but adjusted for sex, age, and race, and the tenfold association found in the 1999 study disappeared.	Defendants argue the tenfold association reported in the 1999 study was regarded by Gorell as "tentative;" the 2004 study is more thorough and shows welders are not at increased risk of suffering PD. Plaintiffs argue the 2004 study parsed variables so finely that the legitimate 1999 results could not possibly have re-appeared; and Gorell remained convinced in 2004 that long-term exposure to manganese confers significant risk of suffering PD.
Lawrence Wechsler, *et al., A Pilot Study of Occupational and Environmental Risk Factors for Parkinson's Disease,* 12 NeuroToxicology 387 (1991).	This early case-control study asked 56 people, 34 of whom had PD, about their work history, personal and family medical history, exposure to certain substances, and so on. The study found that 16% of those who had PD were welders, while none of those who did not have PD were welders.	Plaintiffs argue this study shows a strong link between welding and PD. Defendants argue the small number of persons studied means the results can carry no significance; also, the welders reported exposures to other substances or occupations linked to PD (e.g., aluminum, farming), undercutting the manganese/PD link.

Epi-Study	Summary of Study Results	Arguments
Andreas Seidler, *et al., Possible Environmental, Occupational, and other Etiological Factors for Parkinson's Disease: A Case Study in Germany*, 46 Neurology 1275 (1996).	This case-control study asked 1135 people, 380 of whom had PD, about their occupational history and also their exposure to a variety of substances. After translating occupational history into a "job exposure matrix," the study reported there was no association between PD and an occupational history that included welding.	Defendants argue this study shows welders are not at increased risk of suffering PD. Plaintiffs mine the study data for self-reported exposures, as opposed to the job exposure matrix based on occupational history, and show that persons who reported manganese exposure had a tenfold increased likelihood of suffering PD. Defendants respond that plaintiffs' data-mining techniques are not reliable.
Brad Racette, *et al., Prevalence of Parkinsonism and Relationship to Exposure in a Large Sample of Alabama Welders*, 64 Neurology 230 (2005).	This cross-sectional study examined 1,423 welders in Alabama who believed they might have PD, and determined the numbers of them who probably / definitely ("Pr/De") did have PD. The study then assumed these numbers included *all* Alabama welders who had PD, and calculated the total percentage of Alabama welders who had Pr/De PD. Finally, the study compared this percentage with the percentage of the general population that was found to have Pr/De PD in a 1985 study of an entire Mississippi county. The Alabama welders had a tenfold higher likelihood of suffering PD than the general population in the Mississippi county, and began to suffer PD at a younger average age.	Plaintiffs argue this is overwhelming evidence that welders are at an increased risk of suffering PD, especially given the conservative method of calculating the percentage of all Alabama welders with PD. Defendants identify several alleged flaws in the study, including the overinclusive method of identifying PD, some numbers that seem not to add up, comparison-population differences, and the authors' willingness to conclude only that "[w]e *speculate* that welding exposure either increases the prevalence of PD at all ages or may shift the distribution of PD to a younger age," and calling for more study. *Id.* at 239 (emphasis added).

It is not easy to digest the great mass of epidemiological evidence presented by the parties, much less reconcile the different results of all the studies. This is especially true because defendants and plaintiffs both use the same criticisms to attack studies cited by the other. For example, defendants cite the Coggon study (summarized above), which examined mortality rates due to PD; the Coggon study found PD mortality rates were pretty much the same for welders as for the general population. But, as plaintiffs are quick to point out,

> death rates do not accurately reflect the true distribution of [Parkinson's] disease. The reason is that Parkinson's disease is not a direct cause of death. Although in some cases it may be a contributing or underlying cause, Parkinson's disease is recorded on fewer than half of the death certificates of known cases. This underreporting is compounded by variability in diagnostic accuracy and temporal and geographic differences in death statistics reporting.

Caroline M. Tanner *et al., Epidemiology and Genetics of Parkinson's Disease*, in MOVEMENT DISORDERS: NEUROLOGICAL PRINCIPLES AND PRACTICES 140-41 (Watts & Koller eds. 1997). According to plaintiffs, the rate of PD *mortality* is so poor a proxy for measuring the rate of overall PD *incidence*, that the Coggon study proves nothing. In the next breath, however, plaintiffs set forth an unpublished statistical analysis (by Dr. Wells) of PD mortality data collected by the National Center for Health Statistics, arguing it proves that welders, as a group, suffer earlier onset of PD than the general population.[77] Of course, the devil is in the details, discussion of which is beyond the scope of this opinion

[77] PD is an "age-related movement disorder that affects 1 to 2% of individuals older than 60 years of age." Kevin McNaught *et al., Proteolytic Stress: A Unifying Concept for the Etiopathogenesis of Parkinson's Disease*, 53 Annals of Neurology (suppl 3) S73, S73 (2003). The prevalance of PD increases with age, and it is a rare disease in persons younger than 40. Plaintiffs assert that Dr. Wells's analysis shows that welders, as a group, tend to suffer PD at a younger average age. Subsequent to the Court's *Daubert* hearing, plaintiffs submitted yet another epidemiological study, which they assert confirms Dr. Wells's conclusions. *See* Robert M. Park, *et al., Potential Occupational Risks for Neurodegenerative Diseases*, 48 American J. of Industrial Medicine 63, 63 (2005) ("[w]elding had elevated PD mortality below age 65").

(and perhaps beyond the scope of understanding of the average juror),[78] but this example shows how hard it is to tease out whether the limitations of a given study make it unreliable under *Daubert*.

Defendants insist there is absolutely *no* reliable epidemiology supporting the plaintiffs' claim that welding causes, contributes to, or accelerates the onset of PD: every study cited by plaintiffs is fatally flawed or irrelevant. Defendants thus assert the Court should prohibit admission of all of plaintiffs' epidemiological evidence and conclude, as a matter of law, that plaintiffs cannot show a causal link between welding and PD. There is certainly precedent for this type of ruling. *See, e.g., General Elec. Co. v. Joiner*, 522 U.S. 136, 145-47 (1997) (affirming the district court's exclusion of all four of plaintiff's epidemiology studies, on the basis that none of the studies supported plaintiff's experts' conclusion that exposure to PCBs can cause lung cancer); *Allison v. McGhan Medical Corp.*, 184 F.3d 1300, 1315 (11th Cir. 1999) (affirming the district court's exclusion of plaintiff's four epidemiological studies, because none supported the conclusion that plaintiff's multiple ailments were caused by her silicone breast implants). Defendants conclude by invoking, as a cautionary tale, two other mass tort MDLs – *In re: Silicone Gel Breast Implants Prods. Liab. Litig.* (MDL No. 926), and *In re: Bendectin Prods. Liab. Litig.* (MDL No. 486). In both of these cases, plaintiffs initially obtained large verdicts and/or forced large settlements that proved nearly ruinous to the defendant manufacturers; eventually however, epidemiological studies exonerated the products at issue.[79] Defendants entreat the Court not to allow this MDL to follow a similar

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[78] The Court does not at all mean to impugn the intelligence of the average juror; however, even the smartest and most attentive juror will be challenged by the parties' assertions of observation bias, selection bias, information bias, sampling error, confounding, low statistical power, insufficient odds ratio, excessive confidence intervals, miscalculation, design flaws, and other alleged shortcomings of all of the epidemiological studies.

[79] *See Meister v. Medical Engineering Corp.*, 267 F.3d 1123, 1130-31 (D.C. Cir. 2001) (discussing epidemiological studies regarding silicone breast implants); *Raynor v. Merrell Pharmaceuticals Inc.*, 104 F.3d 1371, 1374-77 (D.C. Cir. 1997) (discussing epidemiological studies regarding Bendectin).

path.[80]

Plaintiffs respond that, at the very minimum, at least *some* of the epi-studies they cited are sufficiently reliable and support their theory of general causation. Plaintiffs contend they have done all they need to do at this juncture, which is simply to carry their burden of showing "by a preponderance of the evidence that the[ir] expert[s'] reasoning and methodology is scientifically valid." 29 Wright & Gold §6266 at 276. Plaintiffs also remind the Court that: (1) at this point in the litigation, they are not required to prove their experts' assessments are correct, only that their experts' methodologies are reliable;[81] and (2) in any event, there is no absolute "requirement . . . that a party must offer *epidemiological* evidence to establish [general] causation," so long as other evidence of general causation exists. *In re: Meridia*

[80] Defendants also note that, for plaintiffs to overcome the epi-studies showing no association between PD and manganese, it "requires more than simply stating that the studies are wrong. Mere criticism of epidemiology cannot establish causation." *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 886 (10th Cir. 2005) (citing *Conde v. Velsicol Chem. Corp.*, 24 F.3d 809, 814 (6th Cir.1994)). Of course, the warning works both ways: mere criticism of epidemiology suggesting an association does not *disprove* causation, either, especially where other evidence of causation exists.

[81] *See Ambrosini v. Labarraque*, 101 F.3d 129, 138 (D.C. Cir. 1996) ("Even if the burden placed on the 'gatekeeper' may seem heavy at times, *see, e.g.*, *Daubert*, 509 U.S. at 600-01, (Rehnquist, C. J., concurring in part and dissenting in part), there is nothing in *Daubert* to suggest that judges become scientific experts, much less evaluators of the persuasiveness of an expert's conclusion. Rather, once an expert has explained his or her methodology, and has withstood cross-examination or evidence suggesting that the methodology is not derived from the scientific method, the expert's testimony, so long as it 'fits' an issue in the case, is admissible under Rule 702 for the trier of fact to weigh.").

Prods. Liab. Litig., 328 F. Supp.2d 791, 800 (N.D. Ohio 2004) (emphasis added).[82] Finally, plaintiffs respond to defendants' invocation of the *Breast Implant* and *Bendectin* litigation by noting the pendulum can also swing the other way: "[t]he available data on welding fume suggests that the more appropriate historical analogies are to lung cancer from cigarette smoking and birth defects attributable to thalidomide. Flawed epidemiological assertions similar to the defense's in this case, or too great reluctance to accept evidence of risk from an exposure, likely contributed to tragic public health crises." Brief in opp. at 79 (citing studies).

The Court takes seriously the lessons that may be learned from other mass toxic tort litigations, including Judge Eldon Fallon's observation in *In re: Propulsid Prod. Liab. Litig.*, 261 F. Supp.2d 603 (E. D. La. 2003): "A trial court must function in the present assessing evidence that presently exists." *Id.* at

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[82] *See also In re Hanford Nuclear Reservation Litig.*, 292 F.3d 1124, 1136-37 (9th Cir. 2002) (holding that the district court's requirement that plaintiffs produce epidemiological evidence showing radiation exposure doubled the risk of causing certain illnesses was error because, "[t]o show generic causation, plaintiffs had [only] to establish by scientific evidence that radiation was capable of causing the type of injuries plaintiffs actually suffered," and it is widely recognized that "[r]adiation is capable of causing a broad range of illnesses, even at the lowest doses"); *Kennedy v. Collagen Corp.*, 161 F.3d 1226, 1229 (9th Cir. 1998), *cert. denied*, 526 U.S. 1099 (1999) (even though "litigants and judges could be skeptical about Dr. Spindler's conclusion" that collagen injections can cause lupus, especially in light of the lack of any epidemiological studies, "Dr. Spindler's analogical reasoning was based on objective, verifiable evidence and scientific methodology of the kind traditionally used by rheumatologists," so exclusion of his opinion was improper); *Bonner v. ISP Technologies, Inc.*, 259 F.3d 924, 928 (8th Cir. 2001) ("[P]laintiff must put forth sufficient evidence for a jury to conclude that the product was capable of causing her injuries, and that it did. We have held, however, that '[t]he first several victims of a new toxic tort should not be barred from having their day in court simply because the medical literature, which will eventually show the connection between the victims' condition and the toxic substance, has not yet been completed.' Bonner did not need to produce a mathematically precise table equating levels of exposure with levels of harm in order to show that she was exposed to a toxic level of FoamFlush, but only evidence from which a reasonable person could conclude that her exposure probably caused her injuries.") (citation and some internal quotation marks omitted); *cf., Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 882 (10th Cir. 2005) ("We are not holding that epidemiological studies are always necessary in a toxic tort case. We are simply holding that where there is a large body of contrary epidemiological evidence, it is necessary to at least address it with evidence that is based on medically reliable and scientifically valid methodology.").

615.[83] As Judge Barbara Rothstein has explained, in assessing the landscape of current knowledge about the neurological effects of manganese, the Court must examine the parties' epidemiological evidence in conjunction with other "non-epidemiological lines of evidence" of general causation, including: biological plausability, animal studies, human clinical studies, case reports and case series, medical textbooks, and other treatises. *In re: PPA Prods. Liab. Litig.*, 289 F.Supp.2d at 1242 & 1238-39. The plaintiffs have presented the following, other known evidence:

- Manganese is a well-known neurotoxin.[84]
- A parkinsonian syndrome can be caused by heavy, direct exposure to manganese.[85]
- A parkinsonian syndrome can also be caused by lighter, more indirect exposures to manganese.[86]
- Researchers routinely note that "manganese has been known to produce a parkinsonian syndrome

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[83] Judge Fallon granted defendants' *Daubert* motion to exclude certain expert testimony, stating: "The Court is aware that the future may shed more light on this matter. Medical science may one day determine with sufficient reliability that a causal relationship exists between a sustained prolonged [heart beat] interval and Propulsid but it is not there yet and may never be." *In re: Propulsid Prod. Liab. Litig.*, 261 F. Supp. at 615. *See also Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996), *cert. denied*, 519 U.S. 819 (1996) ("Law lags science; it does not lead it."); *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1202 (11th Cir. 2002) ("Given time, information, and resources, courts may only admit the state of science as it is.").

[84] *See* Caroline Tanner, *Occupational and Environmental Causes of Parkinsonism*, in PARKINSONIAN SYNDROMES 145, 146 (Stern & Koller, eds. 1993) ("[m]anganese was recognized as a neurotoxicant as early as 1837").

[85] *Id.* at 147 ("High-dose exposure to manganese dust typically produces behavioral changes ('manganese madness'), often within months. * * * Over a period of several months, the initial behavioral syndrome is replaced by apathy and parkinsonian signs . . . .").

[86] *Id.* ("[f]ollowing lower-dose exposures, behavioral changes are similar but less dramatic"). *See also* United States Environmental Protection Agency's ("EPA") Integrated Risk Information System's ("IRIS") Report on Manganese, Reference Concentration for Chronic Inhalation Exposure (CASRN 7439-96-5, available at www.epa.gov/iris/subst/0373.htm#refinhal) (reviewing the literature and concluding: "All of the above studies taken together provide a consistent pattern of evidence indicating that neurotoxicity is associated with low-level occupational Mn exposure.").

in exposed individuals."[87]

- Defendants' own epidemiology experts concede that numerous epi-studies show that manganese exposure is associated with parkinsonism.[88]

- Defendants' own neurology experts have written that the parkinsonian syndrome caused by manganese exposure is clinically similar to Parkinson's Disease.[89]

- Doctors regularly mis-diagnose secondary parkinsonisms as PD.[90]

- Standard neurology texts list manganese exposure as one of the "Factors Associated with Increased

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[87] Lawrence Wechsler, *et al., A Pilot Study of Occupational and Environmental Risk Factors for Parkinson's Disease*, 12 NeuroToxicology 387, 387 (1991); *see also* Jon Fryzek, *et al., A Cohort Study of Parkinson's Disease and other Neurodegenerative Disorders*, 47(5) J. of Occupational & Environmental Medicine 466 (May 2005) ("[h]eavy exposure to manganese is associated with a neurological disorder resembling Parkinson's disease").

[88] Defendants' epidemiology expert, Dr. David Garabrandt, testified at the *Daubert* hearing as follows:

> A. * * * manganese is a well-known chemical that has Parkinsonian action. It is one of the few.
> Q. It does? You don't doubt that?
> A. I do not doubt that overexposure to manganese causes Parkinsonism.
> Q. Do you rely on epidemiology to reach that conclusion, sir?
> A. Do I rely on epidemiology to reach that conclusion? Yes, I certainly do.

Daubert hearing tr. at 912; *see id.* at 912-15 (discussing specific epidemiological studies supporting his opinion).

[89] *See, e.g.*, Nain-Shin Chu, Fred Hochberg, Donald Calne, and Warren Olanow, *Neurotoxicology of Manganese*, in HANDBOOK OF NEUROTOXICOLOGY 91, 94 ((Chang & Dyer eds. 1995) ("Chronic manganism causes an extrapyramidal syndrome with features resembling those found in Parkinson's disease, Wilson's disease, and postencephalitic parkinsonism").

[90] Andrew Hughes, *et al., Accuracy of Clinical Diagnosis of Idiopathic Parkinson's Disease: A Clinico-Pathological Study of 100 Cases*, 55 J. of Neurology, Neurosurgery, and Psychiatry 181 (1992); *see also* Andrew Hughes, *et al., What Features Improve the Accuracy of Clinical Diagnosis in Parkinson's Disease*, 42 Neurology 1142, 1145 (1992) ("It is surprising that so many cases were diagnosed as PD but also had atypical features or a possible etiology for another parkinsonian syndrome.")

Risk for Parkinson's Disease."[91]

- The U.S. Department of Labor's Occupational Safety & Health Administration states that a potential symptom of exposure to manganese fume is "Parkinson's (gait disturbances, clumsiness, tremor, speech disturbances, mask-like facial expression, and psychological disturbances)."[92]

- Welding rod manufacturers include warning language on their products about the neurotoxicity of manganese fumes, such as the following:

> Long-term overexposure to manganese compounds may affect the central nervous system. Symptoms may be similar to Parkinson's disease and can inculde [sic] slowness, changes in handwritting [sic], gait impariment [sic], muscle spasms and cramps and less commonly, tremor and behavioral changes. Employees who are overexposed to manganese compounds should be seen by a physician for early detection of neurological problems.

MSDS Sheet, Hobart Brothers.[93]

- Plaintiffs have offered a substantial number of published case reports associating diagnoses of PD or other parkinsonian symptoms with exposure to welding fumes.[94]

This "other evidence" distinguishes this case from cases like *Joiner*, 522 U.S. 136, where the court

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[91] Caroline Tanner, *Occupational and Environmental Causes of Parkinsonism*, in PARKINSONIAN SYNDROMES 145, 146 (Stern & Koller, eds. 1993); *see also* Kathleen Shannon, *Movement Disorders*, in 2 NEUROLOGY IN CLINICAL PRACTICE: THE NEUROLOGICAL DISORDERS 2125, 2134 (4th ed. 2004) ("exposure to welding seems to predispose to earlier onset L-Dopa responsive PD, possibly as a result of manganese poisoning"). To be fair, Shannon later notes that "manganese toxicity is associated with L-dopa-unresponsive asymmetrical parkinsonism with dystonic features," *id.* at 2144.

[92] www.osha.gov/dts/chemicalsampling/data/CH_250200.html.

[93] *See* www.hobartbrothers.com/msds.asp (doc no. 415884).

[94] *See, e.g.*, Ahmed Sadek, *et al., Parkinsonism Due to Manganism in a Welder*," 22 Int. J. Toxicol., 393, 393 (2003) (case study of a 33-year old welder which "lends support to the hypothesis that welding can produce enough exposure to manganese to produce neurologic impairment"); Keith Josephs, *et al., Neurological Manifestations in welders with Pallidal MRI T1 Hyperintensity*, 64 Neurology 2033 (2005) (discussing eight welders with neurological impairment, three of whom had parkinsonian symptoms); William Koller, *et al., Effect of Levodopa Treatment for Parkinsonism in Welders: A Double-Blind Study*, 62 Neurology 730 (2003) (examining 13 parkinsonian welders). *See also In re: PPA Prods. Liab. Litig.*, 289 F.Supp.2d at 1242 ("In considering the non-epidemiological evidence relied upon by plaintiffs' experts, the court finds significant the sheer volume of case reports, case series, and spontaneous reports associating PPA with hemorrhagic stroke in women.").

excluded epidemiological evidence of general causation. In *Joiner*: (1) none of the epi-studies gave any support to plaintiff's theory that the toxic agent at issue could generally cause the type of harm plaintiff suffered; and (2) there was no other, non-epidemiological evidence suggesting that the toxic agent at issue could produce a similar type of harm.[95] In this case, the non-epidemiological evidence cited above lends meaningful support to plaintiffs' experts' arguments that exposure to manganese in welding fumes can cause a parkinsonian syndrome similar to, and sometimes possibly indistinguishable from, PD. And there is at least some epidemiological evidence suggesting the same thing. *See, e.g.*, Brad Racette, *et al.*, *Prevalence of Parkinsonism and Relationship to Exposure in a Large Sample of Alabama Welders*, 64 Neurology 230 (2005); Lawrence Wechsler, *et al., A Pilot Study of Occupational and Environmental Risk Factors for Parkinson's Disease*, 12 NeuroToxicology 387 (1991). For this reason, defendants' request that the Court disallow any general causation testimony linking manganese exposure to PD is not well-taken.

[95] For the same reasons, this case is distinguishable from *Conde v. Velsicol Chemical Corp.*, 24 F.3d 809 (6th Cir. 1994), which concluded plaintiffs could not show general causation in the face of 19 epidemiological studies showing little or no evidence that chlordane caused cancer, and from other cases citing *Conde*.

B. Conclusion.

The ultimate question raised by defendants' PD motion is: Is the sum of the epidemiological and other evidence proffered by the parties sufficiently reliable to support the assertion that exposure to welding fumes can cause, contribute to, or accelerate a parkinsonian syndrome that some doctors will diagnose as PD? The Court concludes that, at least in the abstract as the question is presented here, the answer is yes. Accordingly, the motion must be **denied**.

IT IS SO ORDERED.

August 8, 2005
date

/s/ Kathleen M. O'Malley
Kathleen McDonald O'Malley

Exhibit A – Core Expert Designations & *Daubert* Challenges

	Expert	Designating Party	Designated at Docket No.	Challenged in *Daubert* Motion? (at Docket No.)
1	Rosemarie Bowler	Plaintiffs	419	[Withdrawn]
2	Robert J. Cunitz	Plaintiffs	419	Yes (972)
3	William Ewing	Plaintiffs	419	Yes (972)
4	Kenneth Gartrell	Plaintiffs	419	No
5	W. Michael Hoffman	Plaintiffs	419	Yes (972)
6	Barry S. Levy	Plaintiffs	419	Yes (972)
7	William Longo	Plaintiffs	419	Yes (972)
8	Elan Louis	Plaintiffs	419	Yes (972)
9	Paul A. Nausieda	Plaintiffs	419	Yes (972)
10	Richard A. Parent	Plaintiffs	419	Yes (972)
11	Jerome Roth	Plaintiffs	419	Yes (972)
12	Martin Wells	Plaintiffs	419	Yes (972)
13	Neil Zimmerman	Plaintiffs	419	Yes (972)
14	Rudolph J. Castellani	Plaintiffs	741-42	Yes (255)
15	Glenn W. Harrison	Plaintiffs	863	No
16	Martin Pomper	Plaintiffs	1229	No
17	Nachman Brautbar	Plaintiffs	1177	Yes (255, 972)
18	Stephen Reich	Caterpillar	622	No
19	Laurence Fechter	GE	623	Yes (966)
20	Samuel M. Goldman	GE	623	No
21	David E. Riley	GE	623	No
22	Joel T. Hutton	GE	623	No
23	Ronald F. Pfeiffer	GE	623	No
24	Thomas J. Boll	GE	623	No

	Expert	Designating Party	Designated at Docket No.	Challenged in *Daubert* Motion? (at Docket No.)
25	Francisco Perez	GE	623	No
26	Sheldon Rabinovitz	Select Arc	628	No
27	Fredrick W. Boelter	Lincoln Electric, et al.	633	No
28	Brian T. Buckley	Lincoln Electric, et al.	633	Yes (966)
29	David Eidelberg	Lincoln Electric, et al.	633	Yes (964)
30	Jon P. Fryzek	Lincoln Electric, et al.	633	No
31	David Garabrant	Lincoln Electric, et al.	633	No
32	Karl Kieburtz	Lincoln Electric, et al.	633	No
33	Richard F. Krenek	Lincoln Electric, et al.	633	No
34	Paul Lees-Haley	Lincoln Electric, et al.	633	Yes (968)
35	Art Meiners, Jr.	Lincoln Electric, et al.	633	No
36	David M. Messick	Lincoln Electric, et al.	633	No
37	Charles Null	Lincoln Electric, et al.	633	No
38	C. Warren Olanow	Lincoln Electric, et al.	633	Yes (964, 971)
39	John W. Olney	Lincoln Electric, et al.	633	No
40	Daniel P. Perl	Lincoln Electric, et al.	633	Yes (971)
41	Gordon Sze	Lincoln Electric, et al.	633	No
42	Leslie J. Ungers	Lincoln Electric, et al.	633	No
43	Lisa Walker	Met Life	800	No
44	Peter S. Spencer	Met Life	800	No
45	R. Walter Makuch	Lincoln Electric, et al.	843	No
46	M. Jonathan Stampfer	Lincoln Electric, et al.	1230	No
47	Cary Coglianese	Lincoln Electric, et al.	1236	No